

Female Genital Anatomy

There are multiple anatomical structures which comprise the internal and external female genital tract such as the clitoris, labia minora and corpus spongiosum (vestibular) erectile tissue, peri-urethral glans, urethra, G-spot, Halban's fascia, anterior fornix erogenous zone, pubococcygeus muscle and cervix. There are also multiple non-genital peripheral anatomic structures involved in female sexual responses such as salivary and sweat glands, cutaneous blood vessels and nipples.

The vagina consists of a tube of autonomically-innervated smooth muscle (longitudinal outer, inner circular layer) lined by stratified squamous epithelium and a sub-dermal layer rich in capillaries. The vaginal wall consists of an inner glandular mucous type stratified squamous cell epithelium supported by a thick lamina propia. This epithelium undergoes hormone-related cyclical changes including slight keratinization of the superficial cells during the menstrual cycle. Deep to the epithelium lies the smooth muscles of the muscularis. There is a deeper surrounding fibrous layer above the muscularis which provides structural support to the vagina, and is rich in collagen and elastin, to allow for expansion of the vagina during sexual stimulation. Three sets of skeletal muscles surround the vagina including the ischiocavernosum, bulbocavernosus, transverse perinei and levator ani and pubococcygeus muscles.

The vulva includes the labia minora, labia majora, the clitoris, the urinary meatus, the vaginal opening, and the corpus spongiosum erectile tissue (vestibular bulbs) of the labia minora. The labia majora are fatty folds covered by hair-bearing skin that fuses anteriorly with the mons verenis, or anterior prominence of the symphysis pubis, and posteriorly with the perineal body or posterior commissure. The labia minora are smaller folds covered by non-bearing skin laterally and by vaginal mucosa medially, that fuses anteriorly to form the prepuce of the clitoris, and posteriorly in the fossa navicularis.

The corpora cavernosa of the clitoris measures up to 5 inches in length. The body of the clitoris consists of two paired erectile chambers composed of endothelial-lined lacunar spaces, trabecular smooth muscle and trabecular connective tissue (collagen and elastin) surrounded by a fibrous sheath, the tunica albuginea. The arteries include the dorsal and clitoral cavernosal arteries, which arise from the iliohypogastric pudendal bed. The autonomic efferent motor innervation occurs via the cavernosal nerve of the clitoris arising from the pelvic and hypogastric plexus.

CLITORIS

The clitoris is formed from the tubercle of the undifferentiated common tissue anlagen in the embryo. The clitoris consists of a midline shaft lying in the medial sagittal plane about 2-4 cm long and 1-2 cm wide which bifurcates internally into paired curved crura 5-9 cm long (attached to the under surface of the pubic symphysis). The clitoris is capped externally with a glans about 20 -30mm long with a similar diameter. The glans is covered by a clitoral hood formed in part by the fusion of the upper part of the two labia minora. The erectile tissue of the clitoral shaft consists of two parallel corpora cavernosa surrounded by a fibrous sheath (tunica albuginea). The clitoral cavernosal erectile tissue consists of smooth muscle and connective tissue. The percentage of clitoral cavernosal smooth muscle in age group of 6 months to 15 years was 65 ± 1.5 , in 44 to 54 years was 50 ± 1.2 and in 55 to 90 years was 37 ± 1.3 (ANOVA, $p=0.0001$). These studies, which revealed a strong link between increase in age and decreased clitoral cavernosal smooth muscle fibers, illustrate that aging women undergo histologic changes in clitoral cavernosal erectile tissue which may play an as yet undetermined pathophysiology in age-associated female sexual dysfunction. Because the shaft and

the glans of the clitoris have no subalbuginea layer between the erectile tissue and the tunica albuginea the organ becomes tumescent or swollen with effective sexual stimulation but does not become erect or rigid. Nevertheless, human clitoral erectile tissue has the capacity to develop drug-induced priapism which responds by detumescing following administration of α -adrenergic agonists. The corpora cavernosa of the shaft do not extend into the glans.

Although the erogenous function of this organ has been known since antiquity, remarkably, the detail of its highly vascular anatomical structure is still in dispute. It is formed from the tubercle of the undifferentiated common tissue anlagen in the embryo. In the presence of androgens this develops into the penis while in their absence the clitoris is formed. Current dissections of adult female human cadavers have been interpreted to indicate that the organ is a triplanar complex of erectile tissue with a midline shaft lying in the medial sagittal plane about 2-4 cm long and 1-2 cm wide which bifurcates internally into paired curved crura 5-9 cm long (attached to the under surface of the pubic symphysis) and externally is capped with a glans about 20 -30mm long with a similar diameter.

The erectile tissue of the shaft consists of two parallel corpora cavernosa surrounded by a fibrous sheath (tunica albuginea) and the whole structure is covered by a clitoral hood formed in part by the fusion of the upper part of the two labia minora while the lower parts meet beneath the clitoris. The clitoral cavernosal erectile tissue consists of smooth muscle and connective tissue. Tufan et al utilized computer assisted histomorphometric image analysis to determine the age-associated changes in clitoral cavernosal content of smooth muscle and connective tissue. Human clitorises were obtained from fresh cadavers (age: 11 to 90 years) and from patients undergoing clitoral surgery (age: 6 months to 15 years). The percentage of clitoral cavernosal smooth muscle in age group of 6 months to 15 years was 65 ± 1.5 , in 44 to 54 years was 50 ± 1.2 and in 55 to 90 years was 37 ± 1.3 (ANOVA, $p=0.0001$). These studies, which revealed a strong link between increase in age and decreased clitoral cavernosal smooth muscle fibers, illustrate that aging women undergo histologic changes in clitoral cavernosal erectile tissue which may play an as yet undetermined pathophysiology in age-associated female sexual dysfunction.

The paired, so-called vestibular (vaginal) bulbs of erectile tissue, which have normally been illustrated on either side of the vagina practically as if in the labia minora, are actually closely applied anteriorly on either side of the urethra. In the male the corpus spongiosum is a single tubular structure of erectile tissue that ensheaths the urethra ending internally as the penile bulb and externally as the penile glans pierced by the urinary meatus. The location and extent of the female corpus spongiosum is contentious. It has been described as being the vascular tissue surrounding the female urethra, as the bilateral vestibular bulbs and as the tissue between the bladder and anterior vaginal wall (Halban's fascia). Most authors claim that the clitoris has no spongiosus tissue. However, the extension of the corpus spongiosus tissue into the clitoris has been described by van Turnhout, Hage & van Diest from their dissections and histology of the adult female cadaver. They observed that the bilateral vestibular bulbs unite ventral to the urethral orifice to form a thin strand of spongiosus erectile tissue connection (pars intermedia) that ends into the clitoris as the glans. The corpora cavernosa of the shaft do not extend into the glans.

Because the shaft and the glans of the clitoris have no subalbuginea layer between the erectile tissue and the tunica albuginea the organ becomes tumescent or swollen with effective sexual stimulation but does not become erect or rigid. Nevertheless, human clitoral erectile tissue has the capacity to develop drug-induced priapism which responds by detumescing following administration of α -adrenergic agonists. The earliest attempt to characterise the possible mechanism(s) by which the crura and vestibular bulbs changed from the flaccid to the tumescent state was published first in

diagrammatic form by Danesino & Martella in Italian. Their working hypothesis, based on the early mechanisms suggested for penile erection, was that during sexual excitement smooth muscle polsters ("cushions") in the arteries supplying the two vestibular bodies became relaxed. Those polsters in the draining veins became contracted as did those in the a-v anastomoses. This diverted blood into the lacunae, filling them and creating tumescence. For detumescence, the arterial polsters contracted while those in the veins and a-v anastomoses relaxed, reducing the flow to the lacunae and allowing the blood restricted in them to flow away. Despite this mechanism being published in English for over 23 years, no independent confirmation of either the mechanism or the polsters in the female arteries and veins have yet appeared. It must be regarded as a speculative working hypothesis.

The finding that human clitoral tissue has nitric oxide synthase (NOS) present in nerves and blood vessels suggests that nitric oxide (NO) may be involved in controlling clitoral blood flow as it does in the penis. Park et al have further examined the possible role for nitric oxide in the regulation of human clitoral corpus cavernosum smooth muscle contractility. In this study, cGMP and cAMP hydrolysis by phosphodiesterases were characterized in the high speed supernatant fraction (cytosol) and in partially purified preparations of human clitoral corpus cavernosum smooth muscle cells. Sildenafil was found to inhibit PDE type 5 cGMP-hydrolytic activity, in the crude extract ($K_i=7$ nM) and in partially purified preparations ($K_i=5-7$ nM) in a competitive fashion. Synthesis of cyclic nucleotides was also carried out in intact cells in culture in response to sodium nitroprusside (NO donor) and forskolin (direct adenylate cyclase activator). Intracellular cGMP was increased by 35% in presence of sildenafil (10nM) in intact cells in culture. The results of this study supports a role for nitric oxide in regulation of human clitoral corpus cavernosum smooth muscle tone.

CORPUS SPONGIOSUM

The paired corpus spongiosum, or vestibular bulbs of erectile tissue practically in the labia minora but are actually more closely applied anteriorly on either side of the urethra. The extension of the corpus spongiosus tissue into the clitoris has been described. The bilateral vestibular bulbs unite ventral to the urethral orifice to form a thin strand of spongiosus erectile tissue connection (pars intermedia) that ends into the clitoris as the glans.

PERIURETHRAL GLANDS

Unlike the clitoral glans the male glans is pierced by the urethra. It has been suggested that there are really two glans in the female, a clitoral glans) and a glans that surrounds the urethra (periurethral glans). The periurethral glans is defined as the triangular area of mucous membrane surrounding the urethral meatus from the clitoral glans to the vaginal upper rim or caruncle. The periurethral glans is mobile and has been shown to be pushed into and pulled out of the vagina by penile thrusting during coitus.

VAGINA

The vagina is a fibromuscular tube that connects the uterus with the vestibule of the external genitalia. It acts in transport of sperm to the uterus and in expulsion of the newborn.

The vagina is a potential space with its anterior and posterior walls usually in apposition. The vaginal walls can be easily separated because their surfaces are normally "just moist", lubricated by

a basal vaginal fluid (approximately 1ml). In the intermenstruum, basal vaginal fluid can consist of multiple secretions that collect in the vagina from peritoneal, follicular, tubal, uterine, cervical, vaginal, Bartholin's and Skene's gland sources. The vaginal wall consists of three layers – the mucosa, muscularis and adventitia.

The vagina has three layers: the internal mucosal layer, the intermediate muscularis layer and the external adventitial layer.

The internal mucosal layer: had transverse folds, or rugae. The epithelium is nonkeratinized stratified squamous epithelium. The epithelium has no glands so there is no mucus secretion.

The mucosa consists of a thick stratified squamous epithelium devoid of glands. The superficial cells of the epithelium undergo hormone-related cyclical changes such as slight keratinization, or increased glycogen production during the menstrual cycle. In the sexually unstimulated state, vaginal fluid has a higher K^+ and lower Na^+ concentration compared to plasma throughout the phases of the menstrual cycle. The actual basal vaginal transudate that percolates through the vaginal epithelium from the plasma circulating in the capillary tufts supplying the epithelium is modified by the limited Na^+ lumen-to-blood reabsorptive transport capacity of the vaginal epithelial cells. The reabsorption of Na^+ by the vaginal epithelium is presumably the ionic driving force for the reabsorption of the vaginal fluid and maintains its level under basal conditions to the "just moist" condition. Autologous plasma placed in a subject's vagina for up to 5 hours shows increased K^+ and decreased Na^+ concentrations indicating that the epithelium is capable of undertaking such ion transfer in vivo. The basal lubrication is usually not sufficient to allow painless penile penetration and thrusting so an enhancement of the lubrication is essential for coitus.

The lamina propria has many thin-walled blood vessels that contribute to diffusion of vaginal fluid across the epithelium.

The lamina propria of the mucosa contains many elastic fibers as well as a dense network of blood vessels, lymphatic and nerve supply. Transudate from these blood vessels, combined with cervical mucus, provide lubrication during sexual arousal and intercourse. Sexual arousal induces a neurogenic transudate that filters through the labyrinthine pathways of the epithelium and saturates its limited Na^+ reabsorptive capacity. It appears within seconds of successful sexual arousal initially on the surface of the vagina as bead-like droplets which then coalesce to create a lubricative film that can partially decrease the acidity of the vaginal basal fluid. The smooth, slippery quality of the formed fluid is probably due to its pick up of sialoproteins coating the vaginal epithelium from the cervical secretion. On sexual arousal the blood supply to the vaginal epithelium is rapidly increased by neural innervation via the sacral anterior nerves S2-S4 and at the same time the venous drainage is probably reduced creating vasocongestion and engorgement with blood. Vaginal lubrication during sexual arousal does not occur from any increased secretion of vaginal glands (nonexistent), cervical fluid or from Bartholin's glands. The enhanced blood flow is activated by the VIPergic innervation of the large vessels supplying the epithelium and the transudation possibly aided by the CGRP (calcitonin gene regulating peptide) enhanced permeability of the capillary tufts. NPY, neuropeptide Y, a known vasoconstrictor, may be involved in constricting the venous drainage. There appears to be very little NOS in the blood vessels of the premenopausal vagina and none in the postmenopausal. After orgasm or the cessation of sexual stimuli, the continuous lumen-blood transfer of Na^+ by the epithelium slowly reabsorbs the excess fluid of the neurogenic transudate by osmotic drag and resets the vagina back to its just moist basal state.

The vaginal epithelium responds to hormonal changes. Glycogen, stored in the epithelial cells,

reaches maximal levels at ovulation after which time the glycogen-rich superficial layer of epithelium is shed. Breakdown of the glycogen by bacteria in the vagina produces lactic acid, causing the vaginal environment to have an acid pH of about 3. This inhibits growth of other bacteria, bacterial pathogens and fungus. It also limits the time in which sperm can survive in the vagina.

2. intermediate muscularis layer: inner circular and outer longitudinal which is continuous with the corresponding layer in the uterus.

MUSCULARIS

The muscularis, consists of autonomically innervated smooth muscle fibers arranged into an outer longitudinal and inner circular layer. In the basal or sexually quiescent state the smooth muscle of the vagina is active especially perimenstrually when it contracts periodically to expel the uterine/vaginal contents. These vaginal smooth muscle contractions are normally not consciously recognized. They only become obvious if they reach painful, spasmodic levels (dysmenorrheic pain). During arousal to orgasm, there is an increasing vaginal luminal pressure. The smooth muscle layers contain a great variety of classical and peptidergic transmitters including 5HT, nor-epinephrine, acetyl choline, dopamine, VIP, NPY, GRP, TRH, CGRP, somatostatin, substance P, oxytocin, cholecystokinin (CCK) and relaxin, but the exact function of each neurotransmitter is unknown.

ADVENTITIA

The adventitia is rich in collagen and elastic, provides structural support to the vagina, and allows for expansion of the vagina during intercourse and childbirth. Surrounding the adventitia are three sets of powerful pelvic striated muscles (1, superficial- ischiocavernosus and bulbocavernosus; 2, the transverse perineii and 3, deep- the levator ani forming the pelvic diaphragm across the anterior of the pelvis of which the largest medial portion is classified as the pubococcygeus). At orgasm a series of pelvic, clonic, striated muscle contractions occur at approximately 0.8 second intervals which gradually get longer and the contractions weaker. They can last for 5-60 seconds. These contractions are concomittant with the subjective feeling of orgasm. Voluntary contractions of the pelvic striated muscles do not give a feeling of intense pleasure but are often used to enhance arousal. During sexual arousal up to orgasm, individual uterine contractions may occur while at orgasm a series occurs mediated by the sympathetic system via the hypogastric nerve. It has been proposed that sexual satiation in the female occurs only when the orgasmic uterine contractions are intense but there has been no quantitative studies to back up this speculation.

ARTERIAL SUPPLY

The main arterial supply to the vagina arises from the three sources. The upper vagina is supplied by vaginal branches of the uterine artery. A branch of the hypogastric artery, the vaginal artery (also know as the inferior vaginal artery), supplies the middle vagina. Finally the middle hemorrhoidal and the clitoral arteries send branches to the distal vagina.

INNERVATION

Autonomic efferent innervation to the upper two thirds of the vagina is through the utervaginal plexus. Autonomic efferent innervation to the upper two thirds of the vagina is through the

utervaginal plexus, which contains both sympathetic and parasympathetic fibers. Sympathetic efferent fibers from the lumbar splanchnic nerves travel first through the superior hypogastric plexus, and then through the bilateral hypogastric nerves to reach the inferior hypogastric plexuses, and finally the uterovaginal plexus. Parasympathetic efferent input to the uterovaginal plexus is from the pelvic splanchnic nerves. Nerves from the uterovaginal plexus travel within the uterosacral and cardinal ligaments, to supply the proximal two-thirds of the vagina. Autonomic efferent innervation to the lower vagina is carried through the pudendal nerve (S2, 3, 4) which reached the perineum through Alcock's canal. Autonomic afferent fibers from the upper vagina travel through the pelvic splanchnic nerves to sacral spinal cord segments. Autonomic afferent fibers from the lower vagina leave the sacral spinal cord through the pudendal nerve. Somatic sensation exists primarily in the distal one third of the vagina and is also carried by the pudendal nerve to the sacral spinal cord.

URETHRA

The female urethra is a short conduit (approximately 3-5 cm long) running from the base of the bladder and exiting in the periurethral glans area to the outside. For nearly its entire length it is surrounded by numerous venous/sinus channels which constitute the corpus spongiosum of the urethra. This submucosal vascular tissue contributes approximately one third of the normal urethral closing pressure and becomes further vasocongested during sexual arousal converting the urinary urethra into the sexual urethra. Scattered in the lining luminal epithelium are cells containing 5-HT (serotonin). Their function is unknown but they are thought to be chemosensing or mechanoreceptor paracrine cells that release the 5-HT on being stimulated by stretch or luminal chemicals. In the animal urethra, 5-HT sensitizes neural mechanisms. It may be that the stretching or massage of the human female urethra by the thrusting penis during coitus causes the release of 5-HT from the urethral paracrine cells enhancing neural afferent input from the organ.

G-SPOT

The G-spot may be considered a general excitable area along the whole length of the urethra running along the anterior vaginal wall. Grafenberg reported that the digital stroking of the anterior vagina along the urethra, especially in the region of the base of the bladder, sexually aroused female subjects greatly. In a number of women this area swelled up to the size of a kidney bean and projected into the vaginal lumen. The G-spot may be considered a general excitable area along the whole length of the urethra running along the anterior vaginal wall. When this is stimulated manually, the sexual arousal induced is almost immediate. This erotic sensitive area is located in closer relation to the bladder base than the urethra. The G spot represents that part of the urethra that contains the periglandular or paraurethral tissue, corresponding to the female equivalent of the prostate. These glands are present to a greater or lesser degree in about 90% of women. In some women, when stimulated sexually, a fluid secretion claimed to be dissimilar to urine or vaginal fluid can be produced which is controversially "ejaculated" from the urethra.

HALBAN'S FASCIA

Halban's fascia is the space between the trigone of the bladder and the anterior part of the vaginal wall. It is filled with mesenchymal lamina, a fibro-elastic sheet made up of collagen, elastic and muscular fibres with a rich blood supply and a nerve supply with Krause bodies or pseudo-corpuseular nerve endings. On stimulation this space becomes vasocongested and creates an erotic

pleasurable response.

CERVIX

The cervix is a relatively insensitive structure. The cervix is a relatively insensitive structure with no erotogenic capabilities per se but it has been implicated by some authors as being important when jostled or buffeted by deep penile thrusting so that the uterus is pushed or rubbed against the peritoneal lining. This is claimed to create sexually pleasurable feelings but in others it creates discomfort. In some women who have had their cervix/uterus removed, a significant loss in sexual arousal and orgasm by coitus occurs. Penile-cervix contact rarely occurs. Penile-cervix contact is not observed in the missionary or face-to-face position but it could occur in the rear-entry sideways and rear-("doggie") positions. An intriguing aspect of the cervix is that it has the second highest concentration of VIP of the female genitals yet no function has been ascribed to the Vipergeric innervation. Its possible role in the secretion of mucus by the infolded crypts of the cervical epithelium has not been investigated.

UTERUS

The uterus, composed of three layers of smooth muscle, is situated in the lower pelvic part of the abdomen. The motility patterns of these organs, especially during sexual arousal to orgasm, have been studied infrequently, rarely measured and are poorly characterised [40, 58, 59, 69, 70, 71]. Their activity is usually monitored either by small luminal balloons or pressure catheters or by electrodes (needle or surface) that pick up the electromyographic activity (EMG) that increases when the muscles contract [69]. Because of the setting of the vagina, smooth muscles amongst striated, contraction of either or both will influence the pressure motility pattern obtained and the interpretation of the records often relies on the fact that at orgasm the striated motility dominates. No studies have been published that record simultaneously, but independently, both the striated and the smooth muscle activity thus allowing their interaction to be better interpreted and characterised.

In the basal or sexually quiescent state the striated muscle plays little or no role but the smooth muscle of the uterus and vagina is active especially perimenstrually when it contracts periodically to expel the uterine/vaginal contents. These uterine and vaginal contractions are normally not consciously recognised [40, 71, 72]. They only become obvious if they reach painful, spasmodic levels (dysmenorrhoeic pain). During arousal to orgasm, the few records obtained show an increasing vaginal luminal pressure [40]. At orgasm a series of pelvic, clonic, striated muscle contractions occur at approximately 0.8 second intervals which gradually get longer and the contractions weaker [58, 69]. They can last for 5-60 seconds. These contractions are concomittant with the subjective feeling of orgasm. Voluntary contractions of the pelvic striated muscles do not give a feeling of intense pleasure but are often used to enhance arousal. Few records of the intrauterine pressure exist and those that do could well be influenced by the size of the devices used to measure the intrauterine pressure (see Levin [40] for discussion). During sexual arousal up to orgasm, individual uterine contractions may occur while at orgasm a series occurs mediated by the sympathetic system via the hypogastric nerve. These have been implicated by some to be important in rapid sperm uptake into the uterus/fallopian tubes but this ignores the effect of vaginal tenting on cervical elevation from the ejaculated pooled semen (see previous section on cervix and Levin [59] for discussion). It has been proposed that sexual satiation in the female occurs only when the orgasmic uterine contractions are intense but there has been no quantitative studies to back up this speculation.

Two studies have reported that vaginal distention induced by rapid increases in volume by inflation of luminal balloons cause i) contractions of the bulbocavernosus and ischiocavernosus muscles [73] and ii) an increase in the velocity of clitoral arterial blood interpreted as an increase in flow [74]. The volume increase used was between 100 to 300ml although the normal volume of the human penis is about 70 ml. Thus penile volume per se would have little effect, but penile thrusting would stretch the vaginal walls and cause the reflex actions. The enhanced clitoral flow and its engorgement and introital tightness around the penile shaft are all features suggested to enhance the pleasure of coitus for both male and female partners.