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Anatomy and physiology of Women's Sexual Function
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Chapter 19
Anatomy and physiology of Women's Sexual Function

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This chapter summarizes the anatomy and physiology of women's sexual response with a clinical perspective. The neurobiology of sexual function in women will be only briefly mentioned for sake of concision. More attention will instead be given to the anatomy and physiology of external genitalia and female organs, which will be summarized focusing on what clinicians should consider while examining the patient complaining of FSD.

The sexual brain

The limbic system and the neo-cortex

A normal sexual response requires the anatomic and functional integrity of the brain's entire limbic system, rather than a particular anatomic structure within it [1]. The limbic system is part of the so called "paleo-cortex" : a comprehensive network involving the hypothalamus and the thalamus (both within the diencephalon), the anterior cingulate gyrus, and many structures of the temporal lobes, including the amygdala, the mammillary bodies, the fornix, and the hippocampus, a phylogenetically ancient type of cortex [1 -4].

Together with the prefrontal lobe, which has a predominantly inhibitory role over the basic instinctual drives, the limbic system is essential in both sexes for the initiation of sexual desire and related sexual phenomena [1,5-7]. Its function activates sexual fantasies, sexual daydreams, erotic dreams, mental sexual arousal, and the initiation of the cascade of neurovascular events triggering all of the somatic and genital responses of sexual function as well as the associated socially appropriate behaviors [7-9]. It is thought that the amygdala maintains a key role as the control center for the four "basic emotional command systems" described by Panksepp: the seeking appetitive-lust system, the anger-rage, the fear-anxiety and the panic separation distress [5]. All these systems may interact to modulate the final perception of sexual desire and central arousal and correlated sexual behaviours. The disruption of any level of the limbic system may cause sexual dysfunction in both sexes, particularly in the domains of desire, central arousal, and socially appropriate sexual behavior [1,5,9-11].

The neo-cortex is increasingly involved in the sexual response in human, first as final target of sensory inputs which arrive from the different sensory organs. Different smells, tastes, words, sights or touch stimuli may activate both the pertinent sensory cortex and the limbix sexual cortex when the signal is "coded" as sexual. Cognitive factors are also in play in evaluating the sexual stimulus and modulate the "judgmemt" of concomitant risks and wishes before engaging, or not, in a specific sexual behaviour [1,10,12].

Neurotransmitters

In men and women, the sexual response is coordinated by the same neurotransmitters, with the most studied being monoamines (dopamine, norepinephrine, and serotonin), neuropeptides (opioid peptides), neurohormones (oxytocin and vasopressin) and neurotrophins (including the Nerve Growth Factor, NGF, which increases in the brain and peripheral blood when people fall in love) [1,6,7, 9,13]. Regional and quantitative differences in neurotransmitter's activities

reflect brain sexual dimorphism that is modulated by prenatal and postnatal endocrine milieus and their interactions with environmental factors [1,5, 6, 14].

Sexual dimorphisms

Many aspects of adult sexual life, both functional and dysfunctional, can claim their origins in the very earliest steps of "sexual dimorphism" [1,5,6,9,14] The gene sequences of chromosomes have two functions: the ability to replicate, termed the "template" function, and the expression of genes, called "transcription." The process of activating and expressing genes results in the genotype becoming the phenotype—i.e., the transformation of the potential, virtual DNA code into actual, functional tissue [1,5]. Interestingly, the "default" phenotypic expression for the human organism, including its brain, is female [1]. Unless a specific substance called testis-determining factor (TDF) is expressed by a short sequence of genes on the Y-chromosome during the maturation process of the fetus, every baby born would have a female brain and body structure [1,9].

The neurons of men and women share all the basic anatomic and functional characteristics. Similarly, neurotransmitters, neurohormones, neuropeptides and neurotrophins have exactly the same structure and roles in both men and women, with some quantitative differences as well as some variability in regional distribution [1,5-7,9,14]. Even the potential for neuroplasticity—i.e., the ability to increase and modulate connections among neurons through neuronal sprouting and the creation of dendritic spines, and the morphological correlate of psychoplasticity—is shared equally in both genders. It appears, then, that the major neurologic differences between men and women lie mainly in their respective degrees of brain dimorphism, i.e. in the differences caused by the action of testosterone on the brain. Quite interestingly, many of the central nervous system effects of testosterone are mediated by estrogen, as a result of the aromatization of testosterone by the enzyme aromatase [1,5,6].

Sexually dimorphic variations in overall brain weight (which is higher, on average, in men) do not appear to be of importance in human sexuality. Quality of brain functioning, sexual and non-sexual, depends on the complex pattern of connections between cells, their continuous plasticity, and the intensity by which they are stimulated through affective events, educational level, and environmental challenges (8-10).

Clinical relevance of brain dimorphism

Hemispheric asymmetry and brain dimorphism have manifest implications in male and female sexual function. For example, the most important sexual cues in women for increasing mental arousal—as well as the mental awareness of that arousal—typically involve verbal intimacy, such as having her partner's receptive and attentive ear, or having affectionate or erotic words spoken to her. Men, on the other hand, rely much more strongly on visual stimulation, either in reality or fantasy, for mental and genital arousal. Much disappointment and frustration results when these two primary sexual cues are polarized in a couple; the consequent mental dissatisfaction may then potentially contribute to sexual dysfunction and even to sexual avoidance [9, 12,15].

Another main neuroanatomical difference between men and women lies in the medial preoptic area of the hypothalamus, the key center of the autonomic nervous system in both sexes [1,6]. Located within this region is a set of nuclei known as the interstitial nuclei of the anterior hypothalamus (INAH) that express their products in a "tonic" or relatively continuous secretory state in men, while they exhibit a "cyclic" pattern of secretion in fertile, ovulating women. This variability has many important consequences on brain function and sexual behavior as well as many other somatic effects. Notably, while the hypothalamic hormone oxytocin is the primary

peptide in female sexual circuitry, the male sexual cycle is most represented by vasopressin [1,6,7,9] .

"Need detectors" located within the hypothalamus are responsible for the activation of the four "basic emotional command systems" of the brain: seeking, rage, fear, and panic [1,5]. These hypothalamic detectors are typically switched on and off by different hypothalamic regions. Prefrontal connections also influence the hypothalamic detectors, typically to inhibit the basic drives [1,4, 5,10,11]. Many additional cognitive and perceptual inputs and cues serve to regulate the basic emotional command systems, as well.

The hypothalamic dimorphisms correlates with gender related reproductive and sexual behaviours. For example, male sexual behavior is typically stable over the entire adult male lifespan; this may potentially be explained by a typical male's lifelong production of testosterone at a relatively tonic, constant rate (notwithstanding the gradual decrease in serum levels that has been described from the second decade of life onwards). In contrast, the physiology of female sexuality is highly discontinuous, both during the regular menstrual cycle as well as during major reproductive life events such as pregnancy, puerperium, abortion, and menopause [9,15,16-18] .

Interestingly, it has also been shown that while receptivity to pheromones remains relatively stable over life in men, there is a peak in pheromone receptivity during ovulation in women, as well as an overall greater level of odor discrimination ability during the years of fertility. After menopause, odor discrimination ability in women decreases significantly and much resembles physiologic male levels [19]. Pheromones may be responsible for mediating interactions in the mid-cycle variations observed in women, which may in turn be triggered by the ovulatory androgen peak, promoting the atresia of non-dominant follicles in the ovary as well as a mental and physical peak in sexual desire, arousability and receptivity [20]. The biologic ramification of these relationships is to increase female sexual responsiveness when the likelihood of conception is at its highest. Human pheromones and their role in sexual attraction and reproduction has been recently reviewed [20].

Central nervous system dimorphisms may well represent the biological basis for the differences in sexual desire, perception, and expression experienced by men and women, including the disparities in the frequency, content, and intensity of erotic fantasies, nocturnal erotic dreams, and sexual daydreams; the perception of central arousal; the quality and quantity of expression of the sexual response, and the likelihood and emotional resonance of orgasm [1, 6-9, 12, 15-18, 21-27].

A more dynamic understanding of the continuous interactions between the somatic body and the psychic mind and how these processes differ between men and women will help to clarify the similarities that are neglected by the polarized focus on contextual factors in women and on biological factors in men.

Neural pathways

At the level of the spine, the neural pathways of sympathetic and parasympathetic sexual responses in both genders follow the same anatomic distributions until their termination in different male and female target sexual organs [1,2,3,9,28]. These pathways involve: the superior hypogastric plexus, the middle hypogastric plexus (which gives rise to the hypogastric nerves joining the testicular or ovarian plexus), the ureteric plexus, the internal iliac arterial plexus, the inferior hypogastric plexus (which receives mostly sympathetic afferent and efferent fibers from the hypogastric nerves, the postganglionic sympathetic fibers derived from the sacral splanchnic nerves, and the parasympathetic fibers derived from pelvic splanchnic nerves—the

nervi erigentes in both sexes—that have their cell bodies in the S2, S3, and S4 segments of the spinal cord) [2,9,28].

The uterovaginal plexus is simply the terminal ramifications of the lower part of the inferior hypogastric plexus. In women, the uterovaginal plexus supplies the uterus, salpinges, ovaries, vagina, erectile tissue of the clitoris and vestibular bulbs (via the cavernous nerves of the clitoris), urethra, and greater vestibular glands [2,28]

In both genders, the perineum receives its primary somatic innervation from the pudendal nerve (derived from S2, S3, and S4) and its sympathetic innervation from the sacral portion of the sympathetic chain [2, 28, 30-32]. The anatomic pathway of the pudendal nerve is very similar in both men and women, forming a single trunk that runs approximately 1 cm posterior to the ischial spine through the greater sciatic foramen inferior to the piriformis muscle. It then re-enters the pelvic cavity through the lesser sciatic foramen and proceeds anteriorly through Alcock's canal, passing posterior to the junction between the ischial spine and sacrospinous ligament and anterior to the sacrotuberous ligament and medial to the internal pudendal vessels. At this point, the pudendal nerve branches into its three main pathways: the inferior hemorrhoidal nerve, the perineal nerve, and the dorsal nerve of the clitoris in women, or penis, in men.

These similarities in neural pathways have important implications for oncologic surgeries, in which the sparing of the vesical nerve plexus fibers that accompany the vesical artery to the bladder may significantly reduce sexual and urinary morbidity in both men and women [9].

They may as well help explain the equal risks of numbness, reduced sensibility, and arousal difficulties of the external genitalia secondary to compression of the pudendal nerve experienced by both men and women who ride bicycles for long periods of time without adequate protection or frequent position changes [29].

Finally, knowledge of similarities and differences between male and female basic anatomic structures and neurological pathways may contribute to a parallel thinking of pathophysiology of male and female sexual disorders, which could be useful in the clinical practice [2, 9, 28, 30-32].

The external female genitalia

Accurate examination of the female external and internal genitalia is often disregarded in the sexual consultation, particularly when sexual disorders are complained of. Opposite to that, the physical examination can be extremely informative not only on the close interaction between biological and psychosexual factors, but also on the variety of critical information a clinician can get.
The following paragraphs will therefore discuss anatomy and physiology of women's genitalia with a clinical perspective: what the physicians should look for to complete his/her diagnosis on the reported FSD.

The vulva includes mons pubis, clitoris and labia majora and minora, which are the structures that are surrounding the urogenital cleft (the external genitals) [2,28].
Mons pubis is the hair covered area over the pubis bone and forms the anterosuperior limit of the urogenital cleft with the labia majora on both sides and ends posteriorly at the anterior margin of the perineal body.

Clinical relevance:

1) a "male" hair distribution, towards the umbilicus, may suggest an excess of ovarian or adrenal production of androgens. It may be associated to acne, hypertrichosis (when excess hair maintain a female distribution) or hirsutism (when excess hair has a male distribution). These changes may be associated to body image concerns which may contribute to a feeling of sexual inadequacy, contributing to sexual disorders [15];

2) loss of pubic hair may anticipate the menopausal changes; it may be perceived as a sign of inadequate sexual aging and may be associated to vulvar dystrophy, loss of sexual desire and/or of genital arousal [33].

Labia majora are the two prominent lateral fatty folds of the urogenital cleft. They meet anteriorly, creating the anterior commissure in front of the glans of the clitoris; and posteriorly forming the posterior commissure. The internal surface has multiple sebaceous follicles which keep the surface lubricated.
The labia minora are smaller, composed of supple elastic skin without subcutaneous fat, but rich in sebaceous glands. Anteriorly they form the clitoral prepuce and clitoral frenulum.
Clitoris and the vestibular bulbs form the erectile apparatus of the vulva. The clitoris is a 7-13 cm cylindral structure composed of glans clitoris, corpus clitoris (which is comprised of the paired corpora) and the crura, the deep extensions of the corpora, which diverge under the pubic arch [2,28,34]. The microscopic anatomy of the clitoris is consistent among different subjects. It consists of cavernous tissue with trabecular smooth muscle and collagen connective tissue [34,35], encircled by a thin fibrous capsule surrounded by large nerve trunks [36]. The vestibular bulbs are paired organs of erectile tissue structure located directly beneath the skin of the labia minora.

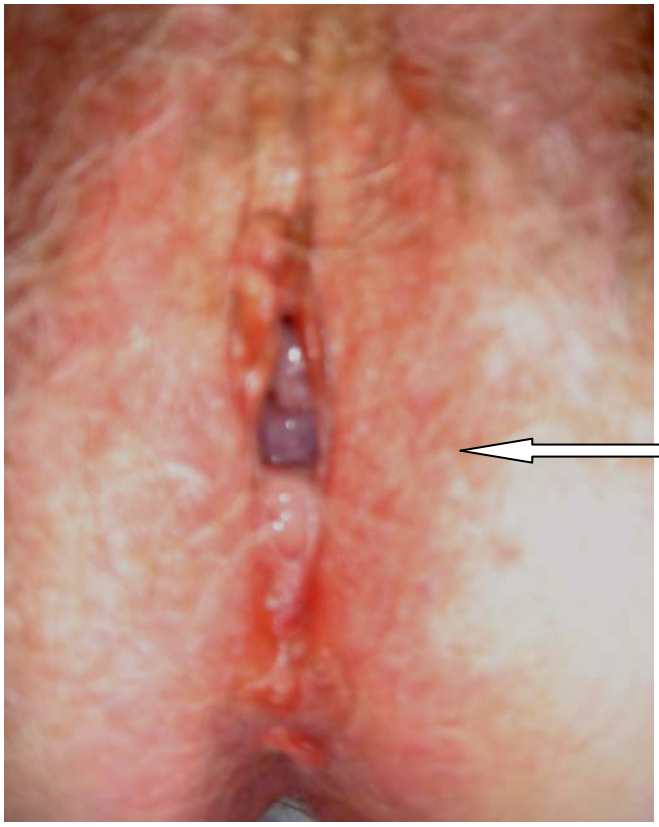
The vulvar vestibule includes the vulvar area comprised between the inferior part of the clitoris, the medial part of labia minora and the fourchette. The central part includes the external side of the hymen, that marks the limit between the vagina, which has a mullerian origin, and the introitus, which has a cloacal origin.

Clinical relevance:

1) Shape of external genitalia and clitoral dimension can vary until the frank anomaly of the intersexual states which may contribute to sexual identity problems and body image concerns [37];

2) Clitoromegaly may be spontaneous or iatrogenic, as consequence of topical and/or systemic treatment with androgens, or with corticosteroids with androgenic activity. It may be associated with a number of clinical conditions, which include the above, plus avoidance of physical contact if the bigger size is perceived as a marker of pathology. When associated to spontaneous or iatrogenic hyperandrogenism, clitoromegaly may be associated to unwanted excess of genital arousal. Persistent, unwanted, intrusive congestion of the clitoris, not associated to increase of sexual desire, may be the objective correlate of the Persistent Sexual Arousal Disorder (PSAD) recently described (see the chapter on arousal) [38].
Priapism of the clitoris, when the glands and the shaft are engorged and painful, is a rear conditions which should be considered in women complaining of "clitoralgia" [9]. Priapism may cause or be associated with pain in the clitoris in non sexual conditions (i.e. it is spontaneous) and/or it can be provoked or worsened when the woman is aroused [9].

3) Atrophy of the clitoris is often associated with lichen sclerosus, an autoimmune pathology characterized by progressive involution of the external genitalia and of the corpora cavernosa [39]. In this condition, the labia minora may disappear and be conglutinated in a unique tissue involution (Fig.1). The vulvar skin becomes thin, pale or white, with loss or the normal papillae, and/ or with area of pathologic cheratinization ("leukoplachia") [33].



Lichen sclerosus, with disruption of vulvar anatomy:
labia majora and minora have been fused in the progressive vulvar involution

Fig.1 Severe lichen sclerosus. Labia minora are almost completely conglutinated, the clitoris is entrapped in the retracted tissue. Severe acquired genital arousal disorder, with acquired anorgasmia and dyspareunia may be the correlated FSD

Courtesy of A. Graziottin, 2006

Mistakenly considered as an "aging" condition, lichen sclerosus may be present in children, adolescents and young women as well (Fig.2). It may be associated to lifelong or acquired genital arousal difficulties, orgasmic difficulties or anorgasmia, introital dyspareunia and acquired loss of sexual desire. A disabling vulvar itching is another key symptom associated to vulvar dystrophy.

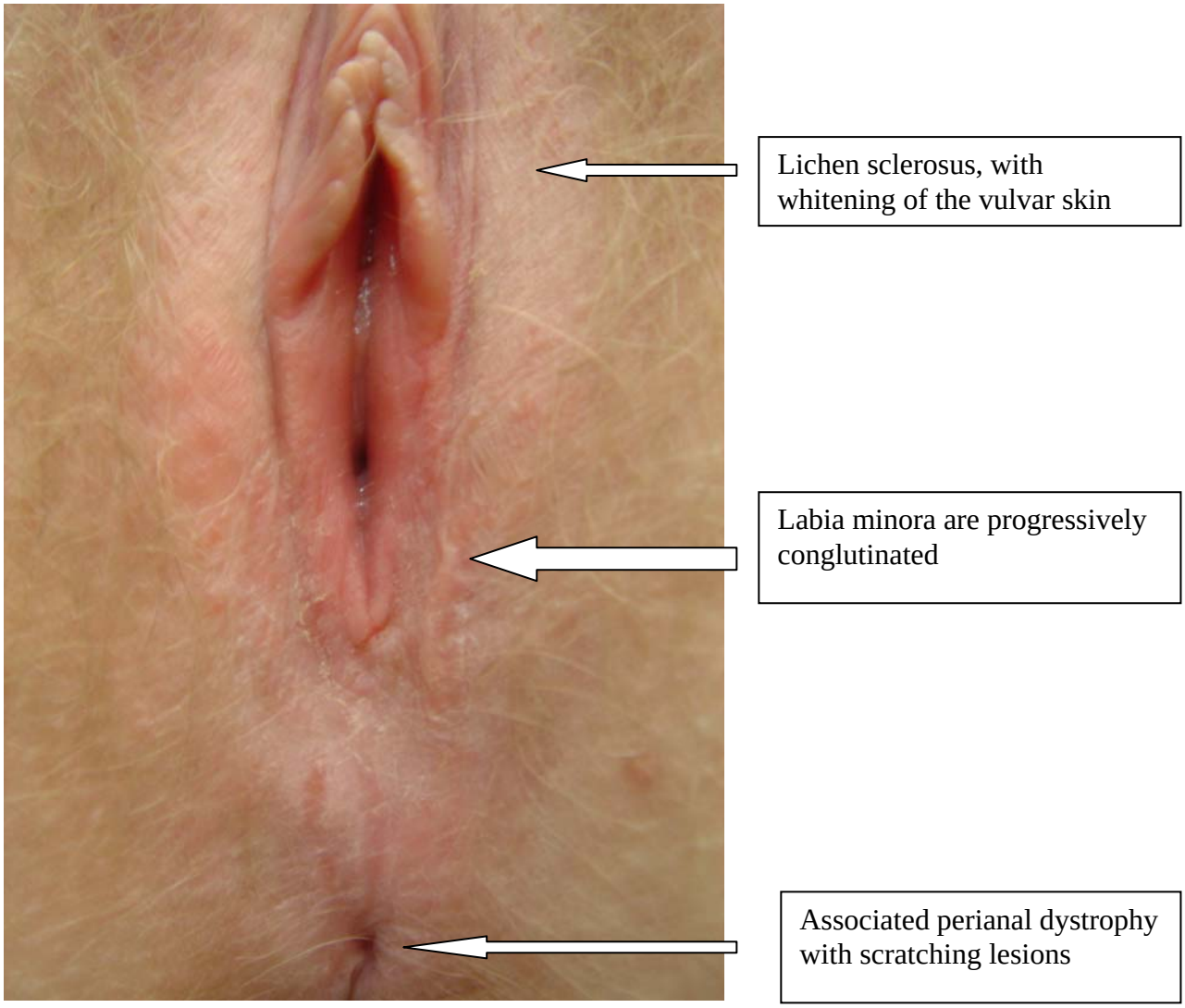
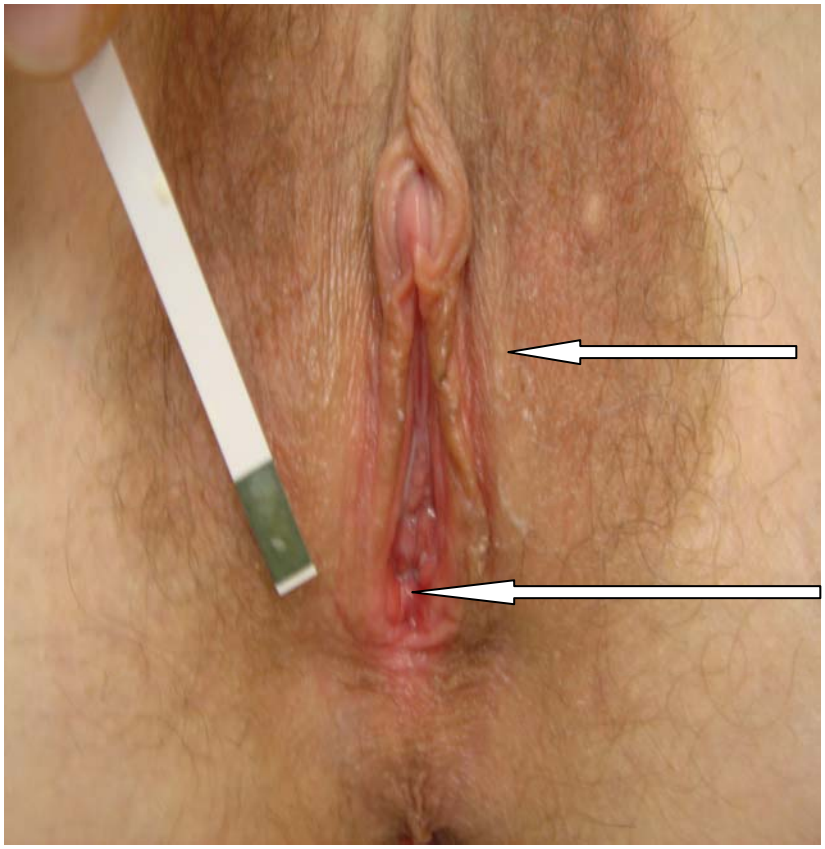


Fig. 2 Progressive lichen sclerosus in a woman 32 years old, complaining of lifelong hypoactive sexual desire disorders and anorgasmia.

Courtesy of A.Graziottin, 2006

Attention to the trophism of the external genitalia is mandatory in all women complaining of acquired genital arousal disorders and/or acquired introital dyspareunia, particularly in the postmenopausal years (Fig.3) [33].



Vulvar aging:
labia majora and minora are involuted, with progressive thinning of the skin

Vaginal aging:
Reddening of the introital mucosa, after a painful intercourse
The vaginal pH is 6.5, as indicated by the stick

Fig.3 Normal aging . Vulvar and vaginal aging in a 57 years old post-menopausal woman, not using hormonal therapy.
She complains of vaginal dryness, difficulty in getting aroused, introital dyspareunia and orgasmic difficulties
Courtesy of A.Graziottin, 2006

4) The skin of labia minora is covered by regularly distributed, soft micropapillae. Irregularly distributed papillae, with harder consistency, are suggestive of papillomavirus (HPV) infections (condylomata). Physiological papillae should be differentiated from condylomata [40]. This sexually transmitted disease requires topically invasive physical and/or pharmacological treatment and may be associated with acquired sexual dysfunctions (vulvodynia contributing to acquired dyspareunia)

5) Retracting scars from episiotomy/rraphy [41], vestibulectomy or perineal surgery [42] may be associated to vaginal dryness, acquired genital arousal difficulties and acquired introital dyspareunia, as pain is the strongest reflex inhibitor of vaginal lubrication.

6) The vulvar vestibule is increasingly involved in inflammatory states (vulvar vestibulitis, VV), with bacterial, mycotic, chemical, neurogenic or allergic etiology [43]. Reddening of the vestibular area is associated to, but not pathognomonic of, vulvar vestibulitis (Fig. 4 and 5). Exquisite tenderness at 5 and 7 of the vaginal introitus, on the external side of the hymen, at the exit of the Bartholin's duct, (looking at the introitus as a clock' face) is a key symptom

of VV, which is the leading etiology of chronic dyspareunia in the fertile age (see chapter on sexual pain disorders).

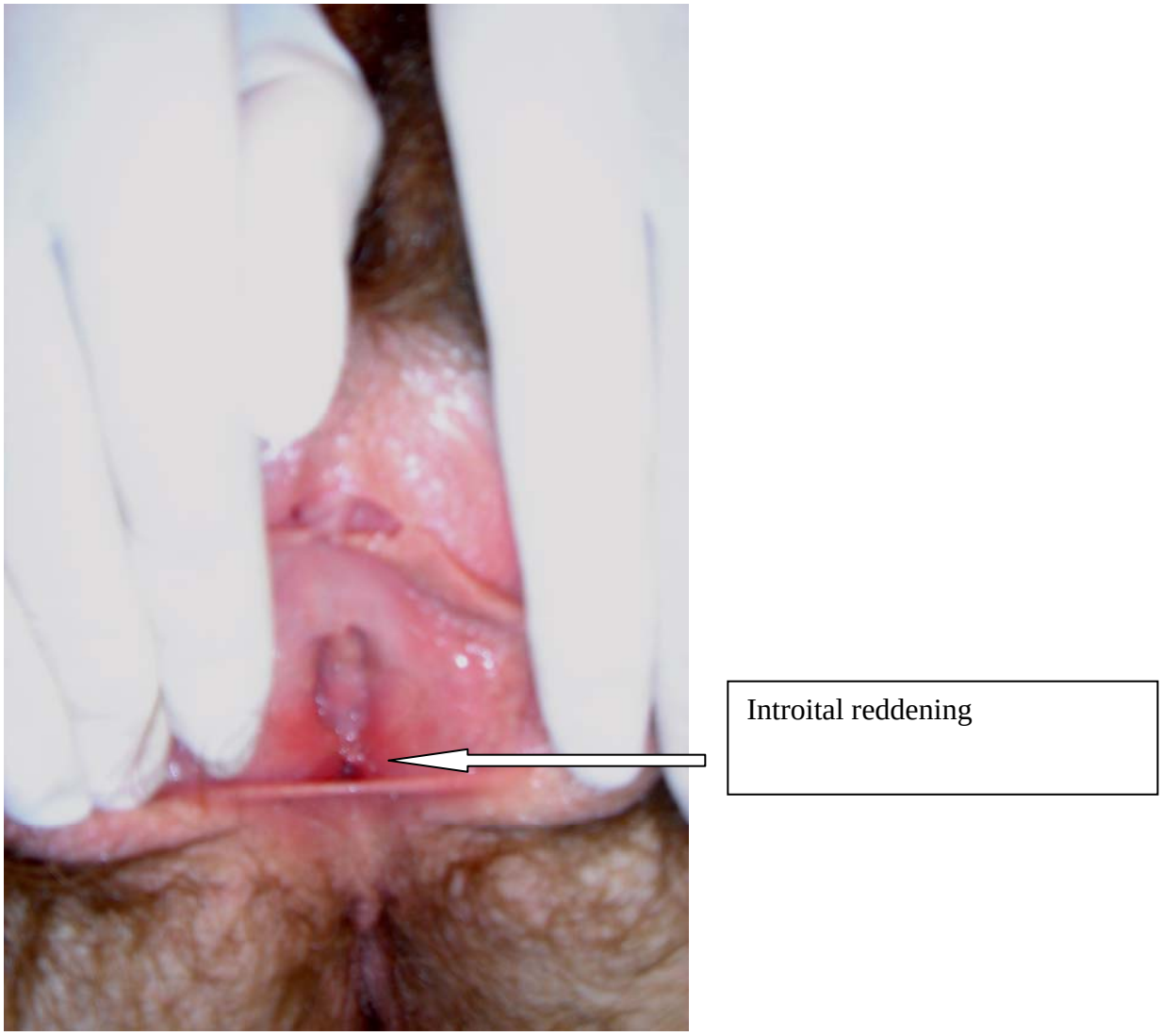


Fig.4 Vulvar vestibulitis: reddening of the introital mucosa is visible at 5 and 7, when looking at the vaginal entry as a clock-face

Courtesy of A.Graziottin, 2006

Fig.5 Vulvitis and Vulvar vestibulitis: diffuse reddening of the introital mucosa is well visible, as the inflammation covers all the area of the vestibule. It extends to the fourchette and part of the centrum tendineum, thus indicating a larger vulvar involvement

Courtesy of A.Graziottin, 2006

7) Reddening of the vulvar region, with oedema, swelling of the labia, itching and pain is caused by candida infection. It causes introital dyspareunia. Recurrent candida is one of the precipitating etiologies of VV. For more details see the chapter on sexual pain disorders.

8) Ritual female genital mutilation (FGM) may be responsible of major changes in the vulvar anatomy (Fig 6).However, after laser de-infibulation the underneath anatomy may appear more maintained than expected when observing the modified genitals (Fig 7). This maintenance may concur to the reported persistence of a normal sexual response, in spite of gross anatomic changes (see chapter on sexual pain disorders), in many women who underwent FMG

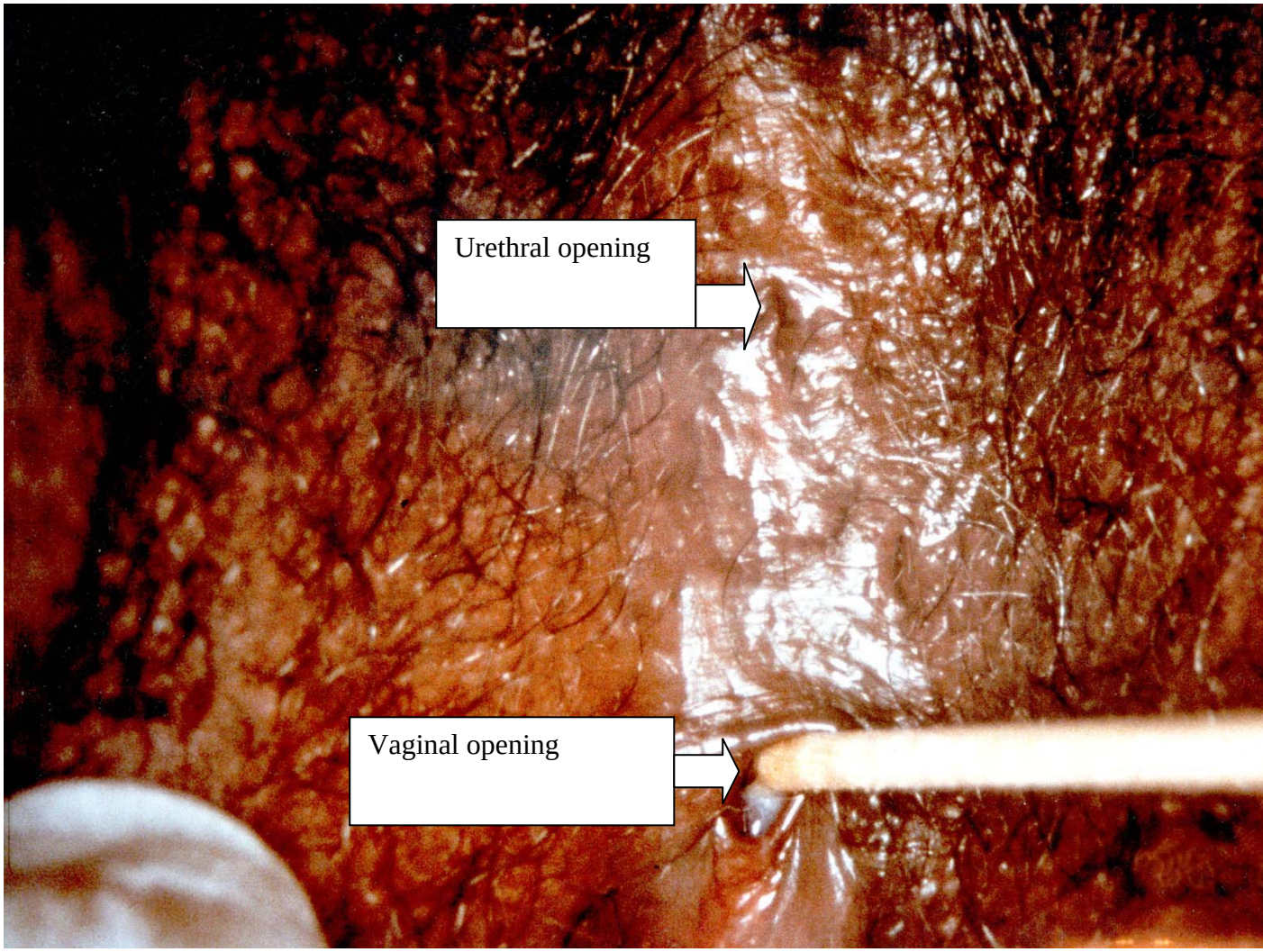


Fig.6 Female Genital Mutilation. The vulvar anatomy is disrupted. The labia have been fused, the glands of the clitoris is no more visible, a tiny opening indicate the vaginal entrance, sufficient only for the menstrual blood to flow

Courtesy of Dr. Lucrezia Catania, 2005

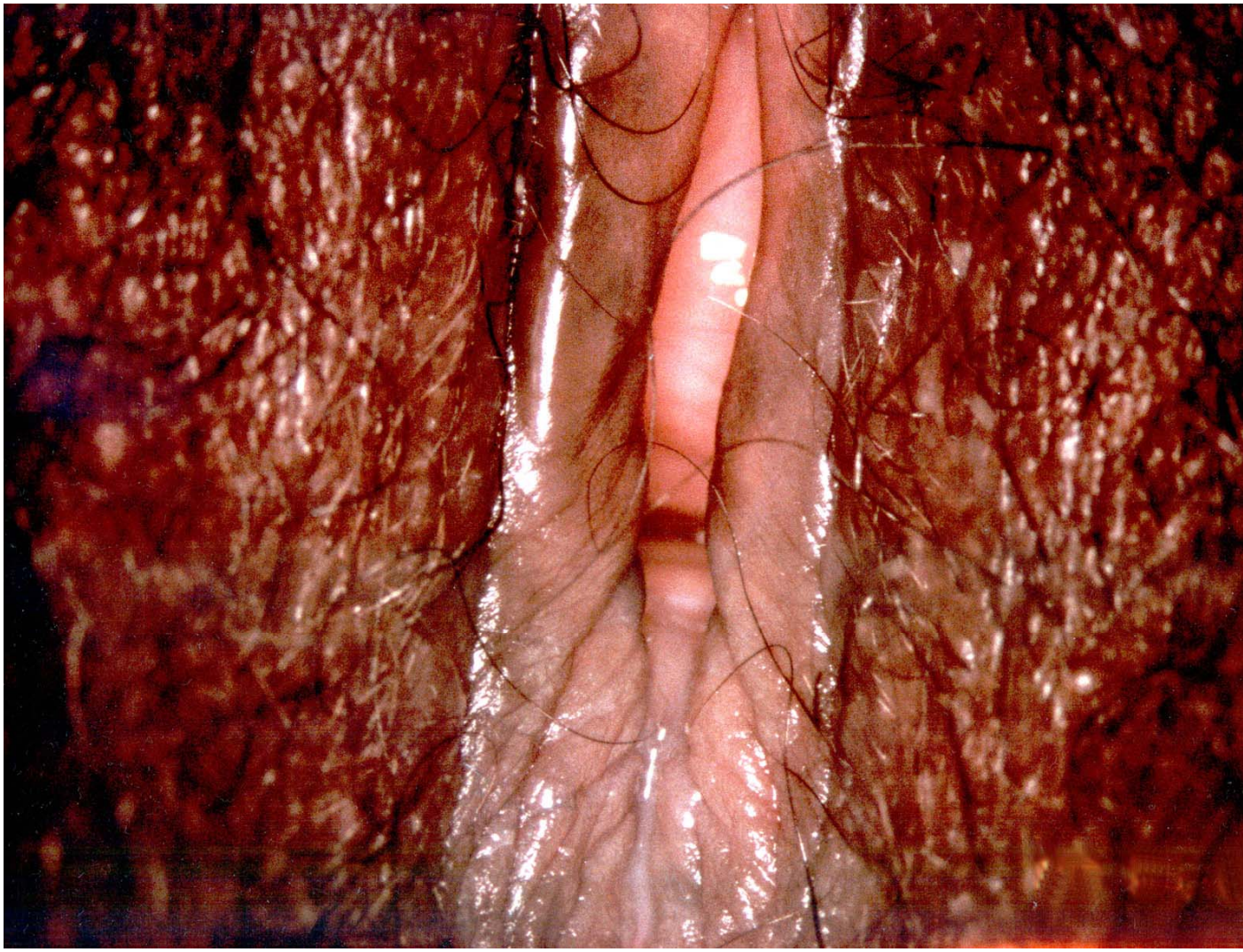


Fig.7 Female Genital Mutilation, after laser de-infibulation. After excision, the vaginal mucosa shows a normal appearance and allows intercourse without pain. Coital orgasm is reported.

Courtesy of Dr. Lucrezia Catania, 2005

The **vagina** extends from the vestibule to the uterine cervix and posterior fornix and connects the uterus with the external genitals. It has four walls and is composed of mucosa (stratified squamous epithelium), lamina propria and the muscularis, which is composed of an outer longitudinally and an inner circular layer of smooth muscle fibers [2,28].
The **hymen vaginae** is a thin fold of mucous membrane, seen just within the vaginal orifice, that varies greatly in appearance. It may be absent, may or may not rupture with sexual activity, or be particularly fibrous and thick, thus contributing to introital dyspareunia. Its remnants after its rupture are the small round "carunculae hymenales" [2,28,34].
The **greater vestibular (Bartholin's) glands** lie deep to the cavernosal bulbs, between those structures and the lateral or outer aspect of the distal vaginal wall [2,28,34].
For descriptive purposes, reproductive organs lying within the body cavity such as ovaries, uterus and fallopian tubes are grouped as **internal genitalia.** The uterus may be involved in the

orgasmic response. However, the research on the effect of hysterectomy on female sexual functioning is not conclusive.

During sexual quiescence, the vagina is a potential space with an H-shaped transverse cross-section and an elongated S-shaped longitudinal section. Grafenberg described the G (Grafenberg) spot of the anterior vagina along the urethra and that stimulation of this spot gave special sexual pleasure and orgasm for the women [44]. Perry and Whipple [45,46] named this sensitive area the Grafenberg, or G spot, in honour of Dr. Grafenberg. Other investigators could not locate a spot, but found, rather than a spot, a general excitable area along the whole length of the urethra running along the anterior vaginal wall [47]. Type 5 phosphodiesterase is expressed in the anterior wall of the human vagina [36,48]. For more details see chapter on orgasmic disorders.

Clinical relevance

The vagina is the key organ of women's physical receptivity. The quality of vaginal trophism is mediated by the level of tissue estrogens [33], which determine: a) the mucosal trophism; b) the vaginal wall elasticity and resistance to coital microtraumas; c) the responsiveness of perivaginal vessels as mediator of the genital arousal, with vaginal congestion and lubrication [22,49,50]; d) the vaginal ecosystem, with the leading Doderlein bacilli, responsible for the maintenance of vaginal acidity at pH around 4, which contributes to the biological defense of the vagina against invasive germs, mostly saprophytic pathogens of colonic origin [33].
The clinical evaluation of vaginal pH (see. fig 1 and fig.3) may help the clinician to diagnose tissue hypoestrogenism and altered ecosystem [33] . The former may contribute to genital arousal disorder (see the pertinent chapter), the latter to dyspareunia (see chapter on sexual pain disorders).

The urogenital triangle and pelvic floor muscles

The pelvic floor muscles in both men and women have the same composition: the pubococcygeous and the coccygeous muscles form the muscular diaphragm that supports the pelvic viscera and opposes the downward thrust produced by increases in intraabdominal pressure. In both genders, the urogenital region consists of superficial and deep spaces created by the bulbospongiosus, ischiocavernosus, sphincter urethrae, and the transversus perinei superficialis and profundus [2,28, 30-32].

In women, the bulbospongiosus surrounds the orifice of the vagina, covering lateral parts of the vestibular bulb. Anteriorly, it becomes attached to the body of the clitoris and similarly compresses the female deep dorsal vein, enabling erection of the clitoral tissue.
The ischiocavernosus is typically smaller in women, and covers the unattached surface of the crura clitoridis, compressing these and retarding the outflow of venous blood during sexual arousal to assist in maintaining clitoral erection. Similarly, the transversus perinei profundus and the sphincter urethrae perform identical functions in both genders [2, 28, 30-32].

Clinical relevance

The integrity of the pelvic floor muscles is important in both sexes [18, 28, 30-32] Comorbidity of urologic, proctologic, and pelvic floor-related conditions adversely influences sexual function in men and women [51]. However, the vulnerability to anatomic and functional damages is higher in women as the result of reproductive events [30-32,41,42]. Lesion of the medial fiber of the pubococcygeus at delivery may cause an impairment of vaginal sensitivity during thrusting, and contribute to postpartum orgasmic difficulties, besides concurring to stress incontinence [30-32,41,42,52]. Defects of the hiatus are responsible for many pathologic entities such as

cystocele, rectocele (Fig. 8), uterine prolaps which may all cause sexual problems for the woman [30-32,41,42,52].
At the opposite end of the spectrum, hyperactivity of the pelvic floor muscles is associated to vaginismus, dyspareunia and vulvar vestibulitis, and to post-coital bladder irritative symptoms such as frequency, urgency and the elusive "urethral syndrome" [42,43]. Co-morbidity between LUTS and dyspareunia is a frequent and still neglected clinical association, with an O.R. of 7.62, according to Laumann et Al [53]. This comorbidity is likely to have in the hyperactivity of the pelvic floor one of its key contributing factors [54] (see the chapter on sexual pain disorders).

Observation and clinical examination of the external genitalia may indicate the tonus of the elevator ani [54]:

a) hyperactivity of the muscle is associated with a retraction of the area between the fourchette and the anus, and is suggestive of vaginismus or acquired dyspareunia and coital orgasmic difficulties;
b) hypotonicity of the muscle is associated with cystocele and or rectocele (Fig.8);

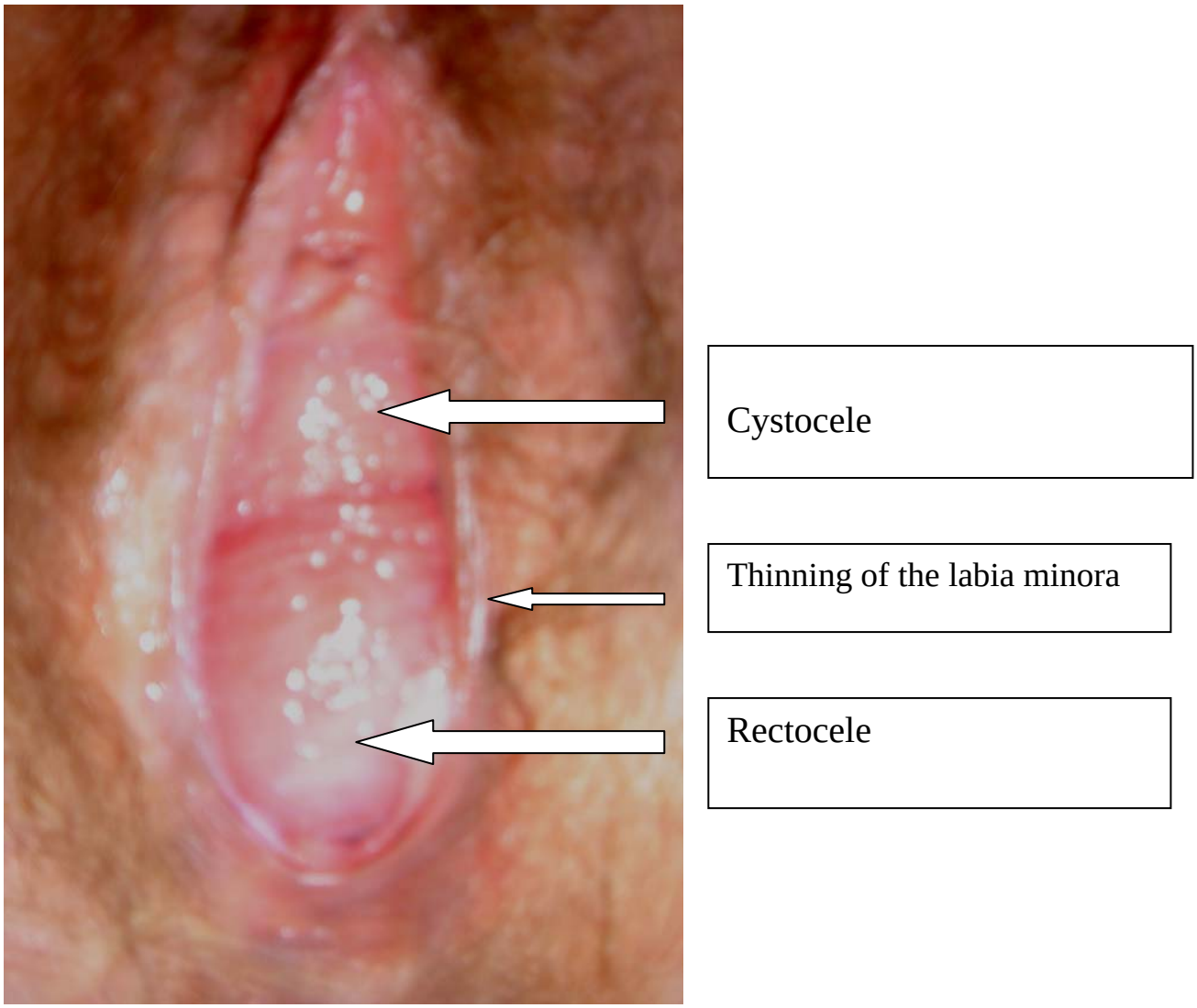


Fig. 8 Cystocele and rectocele in a 65 years old woman complaining of vaginal dryness, lack of vaginal sensations, and anorgasmia. Severe hypotonus of the levator ani is present, in co-morbidity with a moderate stress incontinence

Courtesy of A.Graziottin, 2006

Genital vascular anatomy

The genitals have a rich artery blood supply [2,28]. The labia are supplied from the inferior perineal and posterior labial branches of the internal pudendal artery as well as from superficial branches from the femoral artery. The clitoris is supplied form the ileohypogastric pudendal arterial bed. After the internal iliac artery has given off its last anterior branch, it transverses Alcock's canal and terminates as the common clitoral artery, which gives off the clitoral cavernosal arteries and the dorsal clitoral artery. The proximal (middle) part of the vagina is supplied by the vaginal branches of the uterine artery and the hypogastric artery. The distal part of the vagina is supplied by the middle hemorrhoidal and clitoral arteries (fig.9)[2,28,49,50].

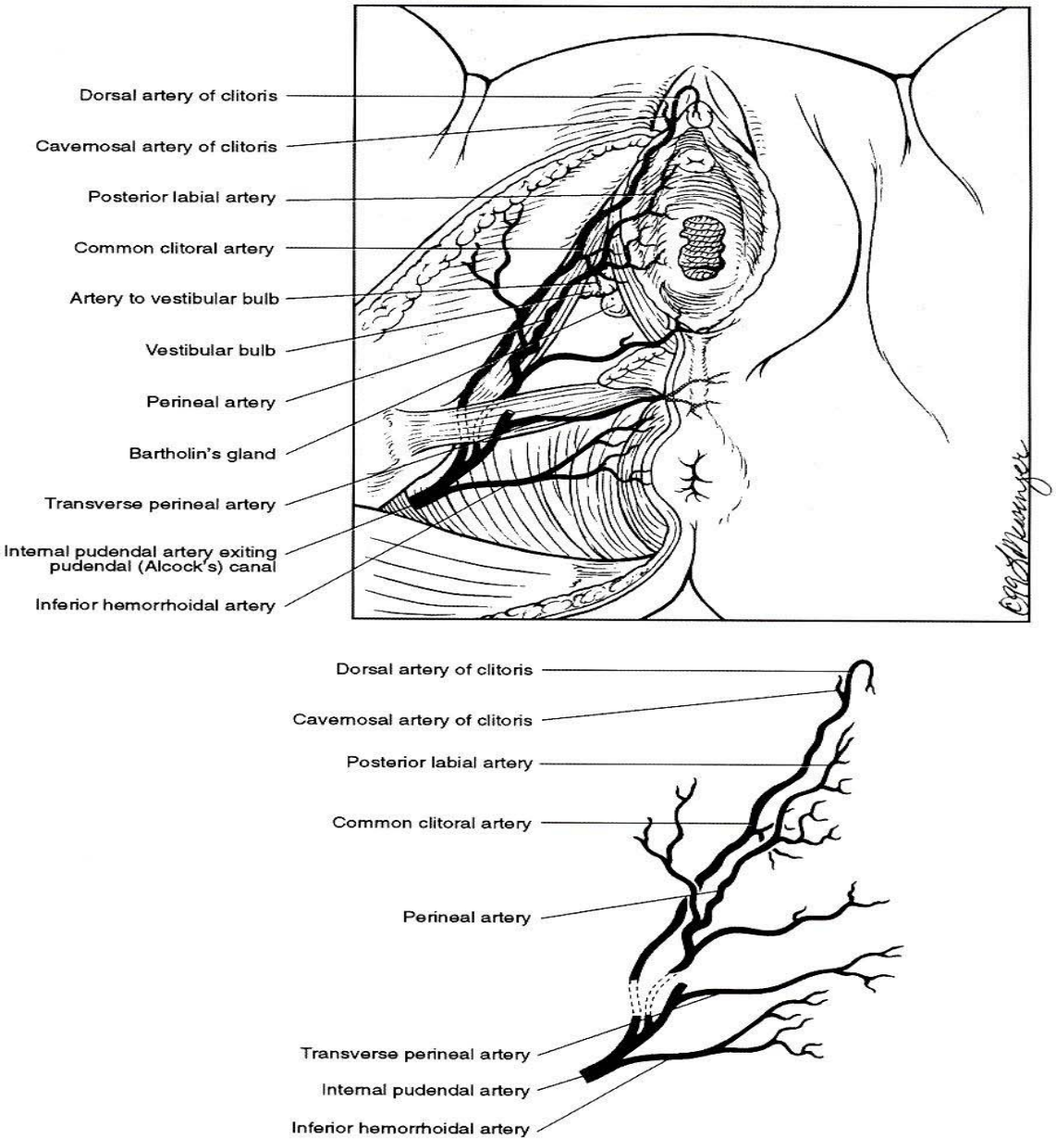


Figure 9. Arterial inflow to the external female genitalia. With permission from (1)

Clinical relevance

The integrity and dynamic responsiveness of vaginal vessels to sexual stimuli, mediated through the neurovascular pathways, is a key contributor of genital arousal response. Factors –such as smoking, cardiovascular diseases, hypertension, diabetes, atherosclerosis - affecting the integrity of vessels may contribute to FSD, specially to genital arousal disorders [55-57] (see also the chapter on arousal disorders)

Peripheral neurophysiology

There is limited understanding of the precise location of the autonomic neurovascular structures related to the uterus, cervix and vagina. Uterine nerves arise from the inferior hypogastric plexus formed by the union of the hypogastric nerves (sympathetic T10-L1) and the splanchnic fibers (parasympathetic S2-S4). This plexus has three portions: vesical plexus, the rectal plexus and the uterovaginal plexus, which lies at the base of the broad ligament, dorsal to the uterine vessels and lateral to the uterosacral and cardinal ligament. This plexus provides innervation via the cardial ligament and uterosacral ligaments to the cervix, upper vagina, urethra, vestibular bulbs and clitoris. At the cervix sympathetic and parasympathetic nerves form the paracervical ganglia. The larger one is called the uterine cervical ganglion. It is at this level that injury to the autonomic fibers of the vagina, labia and cervix may occur during hysterectomy. The pudendal nerve (S2-S4) reaches the perineum through Alcock's canal and provides sensory and motor innervation to the genitalia (fig. 10 & 11).

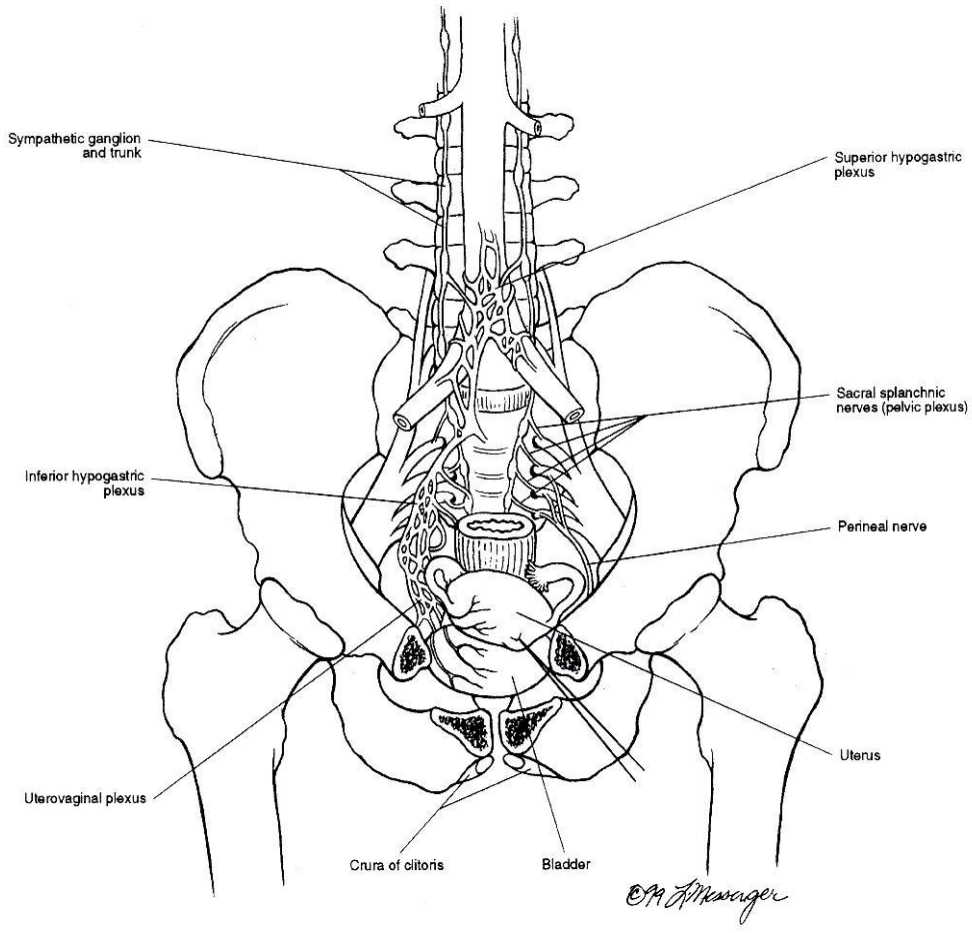


Figure 10. Autonomic and somatic innervation of the female genitals. With permission from (63)

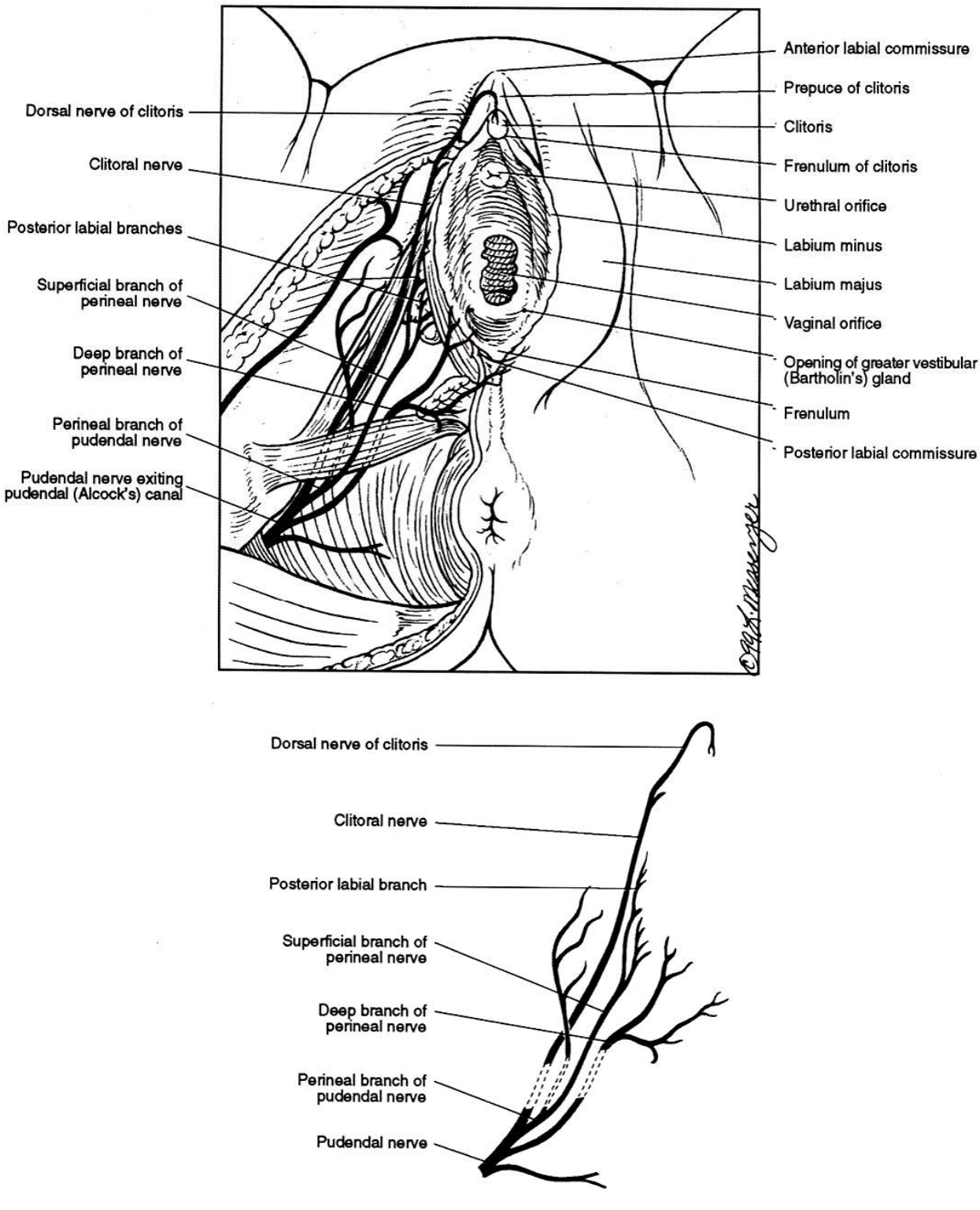


Figure 11. Motor and sensory nerves innervating the external female genitalia. With permission from (63)

As such the anatomic structures involved in the female genital sexual response are innervated by autonomic and somatic nerves. 1) the pelvic nerve issuing from level S2-S4 of the spinal cord (parasympathetic); 2) the hypogastric and lumbosacral chain issuing from level (T12 – L2) of the spinal cord (sympathetic); 3) the pudendal nerve (somatic) with cell bodies of the motoneurons located in the Onuf's nucleus (S2 – S4); and 4) the vagus nerve issuing from the nucleus tractus solitaries. For review see [58].

Sensory stimuli relevant to sexual function are conveyed by afferent pathways consisting of pudendal, pelvic and hypogastric nerves and the lumbosacral sympathetic chain. They relay information to the dorsal horn, medial central and lateral gray matter of the lumbosacral spinal cord, and the vagal afferent fibers convey sensory information from the genital apparatus to the nucleus tractus solitarus (NTS) [58]

Genital physiological response during sexual arousal.

During female sexual arousal the blood flow to the genitals is increased in the clitoris, the labia and the vagina leading to vasocongestion, engorgement and lubrication [22,49,50,58-61]. Furthermore orgasm may involve rhythmic contractions of the pelvic striated circumvaginal musculature, often with concomitant uterine and anal contractions [58]. For more details see chapter on orgasmic disorders

Vaginal lubrication is a consequence of the increased blood flow. During the non-aroused state the anterior and posterior walls are normally collapsed and touch each other. Nevertheless, they do not adhere as they are covered with a thin layer of basal fluid allowing them to separate easily. As such, the fluid is a mixture of secretions from the whole genital tract. This is mainly a vaginal plasma- transudate mixed with desquamated cervical and vaginal cells and cervical secretion. No glandular elements have ever been identified in the normal human vagina [22,49,50]. The vaginal transudate is formed from the blood, slowly circulating through the capillaries supplying the vaginal epithelium. A plasma filtrate from the blood leaks out of the capillaries into the interstitial tissue space. In the vagina the fluid then passes through the epithelium. In the sexually unstimulated state the vaginal fluid has a higher K^+ and lower Na^+ concentration throughout the phases of the menstrual cycle [50]. In the non-sexually stimulated state there is a slow passage through the epithelium and in balance with reabsorption, this leads to the just moist vagina, but not moistened enough to allow penetration without pain. The slow blood circulation also results in a hypoxic lumen with low oxygen tension [22,49,50]. During sexual arousal, the blood flow to the vaginal epithelium is rapidly increased as a consequence of neural innervation via the sacral anterior nerves (the parasympathetic pathway (pelvic nerve) [62]. The increased blood flow results in an increased volume of ultrafiltrate percolating between the vaginal epithelial cells, saturating the reabsorption capacity and thereby the excess of fluid accumulates at the vaginal surface as a clear, slippery and smooth lubricant, moistening the vagina so painless penetration and thrusting is possible. Despite many inaccurate accounts in physiology textbooks, vaginal lubrication during sexual arousal does not occur from increased secretion of vaginal glands.

Activation of the sympathetic nervous system occurs during the later stages of arousal and orgasm and is responsible for the increase in heart rate and blood pressure in women [58].

During the arousal response there is a relaxation of the trabecular smooth muscle in the clitoris and the clitoral blood flow increases. This leads to a rise in intra-clitoral pressure with increased tumescence and engorgement [22, 58-62]. As the tunica of the clitoris is elastic, no veno-occlusive mechanism occurs as it is seen in the penis.

Neurotransmitters of importance for the arousal response.
Several adrenergic, cholinergic and nonadrenergic-noncholinergic (NANC) neurotransmitters/mediators have been identified in the female genital tract (adrenaline, acetylcholine, Vasoactive Intestinal Polypeptide (VIP), nitric oxide synthase, neuropeptide Y, calcitonin gene-related peptide, substance P, pituitary adenylate cyclase activating polypeptide, helospectine and peptide histdine methionine) [22,49,50]. Still there is a lack of knowledge of which mediators are crucial in the regulation of female genital arousal response [50]. Vasoactive Intestinal Polypeptide (VIP) has traditionally been considered the most important neurotransmitter in the regulation of vaginal blood flow [22], but nitric oxide (NO) has also been identified as an important mediator of increased blood flow to the female genitals during arousal based on human and animal studies [36,48]. However, the exact roles of these and other neurotransmitters/ mediators in the physiological and pathophysiological arousal response still need further investigation.

In summary, during sexual stimulation, the genital female sexual arousal response is elicited by sensory stimulation as well as central nervous system activation. This culminates in a series of vasocongestive as well as neuromuscular events leading to physiological changes, as vaginal lubrication, increased length and width of the clitoris, engorgement of the labia as well as increased sensitivity of the genital. All representing the physiological genital arousal response in women.

Conclusion

The re-reading of women's anatomy and physiology with the clinical perspective of an updated sexual medicine is a necessary pre-requisite for a better understanding of biological contributors of women's sexual function and dysfunction. However, for sake of concision, the description in this chapter only covers some aspects of anatomy and physiology of importance for the sexual function in women.
The potential clinical relevance of the physical examination has been stressed with the aim of stimulating a closer examination of the biological conditions potentially associated to FSD.
This is of special relevance when genital arousal disorders, dyspareunia and vaginismus are complained of. However, the clinical examination should be performed in any FSD, as anatomic and/or genital dysfunctional problems may be contributor as well of lifelong or acquired desire and/or orgasmic disorders.

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