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Local Responses to Genital Arousal — Mechanisms of Lubrication

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Abstract

Purpose of Review The aim of this review is to outline the anatomical and physiological processes involved in vaginal lubrication and to examine the current options for its measurement in the laboratory.

Recent Findings The literature suggests that androgens and estrogens play a crucial role in the maintenance of vaginal structure and vascular functions, thereby delivering positive downstream effects on vaginal lubrication. Estrogens and androgens help maintain healthy genital tissue and capillary beds. During sexual arousal, interactions among these hormones with various peptides encourage genital vasocongestion, which, by way of increased pressure on surrounding cells, is believed to facilitate lubrication. Litmus strips and Schirmer Tear Test strips circumvent many pitfalls of previous objective measurements and appear to be viable methods for assessing vaginal lubrication in the laboratory.

Summary Vaginal lubrication is believed to result from increased vasocongestion and appears to be modulated by sex steroid hormones. Preliminary support has emerged for the use of litmus strips and Schirmer Tear Test strips to measure lubrication in response to sexual films in the laboratory, though more research is needed to determine the psychometric properties of these applications.

Keywords Vaginal lubrication · Genital sexual arousal · Vaginal vasocongestion · Sex steroid hormones · Measurement of lubrication · Vaginal transudate

Introduction

Sexual arousal involves both psychological (i.e., subjective) and physiological processes that prepare a woman's mind and body for sexual activity [1]. Subjective sexual arousal includes the "cognitive" [2, 3] and "emotional" [4, 5] experiences of arousal and has been defined as positive mental engagement in response to a sexual stimulus [6]. Physiological arousal comprises both nongenital (e.g., increased heart rate, sweating, pupil dilation, hardening and erection of the nipples, and flushing of the skin) and genital responses, namely vasocongestion and vaginal lubrication.

The production of lubrication is necessary for ease of penetration during sexual activity [7, 8] and appears to facilitate enhanced sexual pleasure for many women [9]. In an unaroused state, the vaginal surfaces are lightly coated with basal fluid that is produced by various glands and epithelia (i.e., the abdominal peritoneal cavity, the fallopian tubes, the uterus, the cervix, the vaginal walls, and Bartholin's glands). Although the basal fluid protects the vaginal canal from adhesions and subsequent infection, the production of additional lubrication is required for painless penetration and thrusting in the absence of a sexual pain disorder [8]. This review outlines the anatomical and physiological processes involved in vaginal lubrication, as well as the measurement of lubrication in the laboratory.

Genital Vasocongestion

During sexual arousal, autonomic nervous system activation leads to an increase in heart rate and blood flow throughout the woman's body. Locally in the genitals, autonomic nerve endings within the vaginal tissue release

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vasoactive intestinal polypeptide (VIP) and neuropeptide Y, both of which have demonstrated key relevance for genital blood flow [10]. VIP freely interacts with nitric oxide to facilitate smooth muscle relaxation [11, 12], thereby increasing vascular inflow through the expanded diameter of the local blood vessels. It is generally thought that the reduction of venous drainage maintains vasocongestion and causes the distal two thirds of the vaginal canal to expand [13••]. Increased vasocongestion is believed to trigger the production of vaginal lubrication, which was observed by Masters and Johnson within 10–30 s after the initiation of sexual stimulation [14].

Mechanisms of Lubrication

Vaginal lubrication occurs primarily within the vaginal canal and minimally on the labial surface. Plasma transudate, the thin fluid produced within the vaginal canal, contains few, if any, cells that have been filtered out of the plasma due to an increase in venous pressure [15]. Mucus produced by the Skene's and Bartholin's glands also provides moisture to the surface of the labia. The Skene's glands, the homologue of the male prostate gland, are located on either side of the urethra and secrete a lubricating fluid that contains biochemical markers such as prostate-specific antigen, human urinary protein 1, and phosphodiesterase type 5 [16]. The Bartholin's glands are analogous to the bulbourethral (Cowper's) glands in males and are located at either side of the external vaginal orifice [17]. Compared to lubrication produced internally in the form of plasma transudate, the lubrication produced by the Skene's and Bartholin's glands is thought to be minimal [14].

During sexual arousal, pressure builds in the vaginal walls as blood surges to the vaginal mucosa (i.e., the first layer of the vaginal tissues, which consists of the epithelium and lamina propria), thereby allowing more transudate to pass through the vaginal epithelium cells (for a review, see [18]). In an unaroused state, vaginal fluid contains relatively high potassium and low sodium concentrations, with additional, notable concentrations of calcium and chloride [19, 20]. However, as increased transudate passes between cells during sexual arousal, sodium transfer gives rise to high concentrations of both sodium and chloride [19]. As the vaginal epithelium cells become saturated with sodium, their limited reabsorptive capacity prohibits the fluid from being reabsorbed back into the cells. As a result, small droplets of plasma move through the epithelium and coalesce on the vaginal surface to eventually form a moist barrier which protects the vagina from tearing during penetration [13••, 18]. Throughout this process, the overall pH of the vaginal canal increases to protect sperm from the acidic milieu of the unaroused vagina [21].

Hormones and Overall Genital Arousal

Sex steroid hormones play a significant role in genital arousal as large quantities of androgen, estrogen, and progesterone receptors are present in vaginal tissue [22]. Estrogens (see [23], for a review) and androgens (see [24], for a review) facilitate genital arousal, while progesterone is thought to blunt the powerful effects of estrogen [25]. In addition to serving as precursors to the biosynthesis of estrogens, androgens bolster the vitality of vaginal tissues and help to maintain healthy vaginal function [26, 27••]. Diminished lubrication is observed in women with androgen deficiencies [28•] and has been shown to improve following dehydroepiandrosterone (DHEA) treatment [29•]. Estrogens are potent sex steroid hormones with vasodilatory and vasoprotective properties that regulate blood flow into and out of the vagina and clitoris. Estradiol, a secreted form of estrogen, modulates the structure and function of genital tissues (as reviewed in [30]). Reductions in estradiol have been linked to reduced vaginal blood flow, which likely results in decreased vaginal lubrication [31]. Progestins, the synthetic form of progesterone, may inhibit smooth muscle cell growth [32] and, in turn, vasodilation and lubrication. Indeed, women taking hormonal contraceptives which contain progestin in addition to estrogen have reported decreased lubrication [33•]. The effect of these hormones on vaginal lubrication is largely thought to be secondary to their effect on the vaginal structure and vascular functions.

Hormones and Vaginal Tissue

The presence of both estrogens and androgens appears to benefit vaginal tissue structure, which likely has positive downstream effects on genital blood flow and lubrication. Estrogens and androgens are responsible for regulating distinct cellular processes within the tissue of the vagina, such as the growth and function of neurons, blood vessels, smooth muscle, and cells within the endothelium and epithelium (for reviews, see [23, 24]). These processes keep the capillary beds lush and vaginal tissue healthy. Estrogen is thought to be particularly important for the maintenance of the vaginal mucosal epithelium (i.e., the outer layer of the vaginal wall) [22, 34]. For example, one study found that estradiol increased the thickness of the vaginal epithelium of ovariectomized rats to a thickness that was *greater* than that of non-ovariectomized rats, whereas progesterone and testosterone did not influence epithelial growth [35]. However, the authors observed that the co-administration of estradiol plus progesterone or testosterone yielded tissue *most similar* to that of non-ovariectomized rats. That is, whereas the

treatment of estradiol alone produced atypical thickening of the epithelium, the co-administration of estrogen and progesterone or testosterone facilitated typical, or comparatively less, epithelium growth. This suggests that progesterone and testosterone may moderate the facilitatory effect of estradiol on epithelial growth.

In a study examining the role of androgens on the maintenance of the vaginal epithelium, twenty-one postmenopausal breast cancer patients were treated with either 150 or 300 µg of intravaginal testosterone daily for 28 days, at which point a vaginal maturation index assessment was performed [36]. The vaginal maturation index assesses the ratio of parabasal (i.e., immature cells that are not affected by estrogen and progesterone) to superficial (i.e., mature cells that have been affected by estrogen) cells in the vaginal epithelium, where greater vaginal maturation index scores indicate a greater amount of estrogen stimulation (for a review, see [37]). In the group of women receiving the 300 µg dose, the vaginal maturation index increased from 20 to 40%, suggesting that topical testosterone facilitated the beneficial effects of estrogen on the vaginal epithelium. Women also reported significant decreases in vaginal dryness over the course of the study. These findings indicate that bioavailable androgens aid estrogen in stimulating vaginal tissue. This improvement in tissue structure likely mediates improvements in vascular function, as fuller tissue allows for a greater density of capillary beds and increased blood supply to the genitals (see [38], for a review). This increased blood supply could, in turn, increase vaginal lubrication.

Functional Modulation of Vasocongestion

Neurotransmitters

Sex steroid hormones also modulate vascular components of vaginal tissue by regulating the activities of neurotransmitters and proteins such as vasoactive intestinal polypeptide and nitric oxide. Adrenergic and non-adrenergic non-cholinergic neurotransmitters mediate non-vascular and vascular smooth muscle contractility, hence playing a crucial role in vasocongestion [39]. Vaginal tissue also has a dense supply of vasoactive intestinal polypeptide (VIP) and nitric oxide (NO) immunoreactive fibers [12, 40]. VIP is a neurotransmitter located in the vasculature of the genitals. Data confirm VIP innervation occurs mainly in blood vessels beneath the vaginal epithelium [41]. Activities of these neurotransmitters appear to be largely hormone dependent. For example, research has shown that VIP fails to increase vaginal blood flow in estrogen-deprived women [42]. Palle et al. (1991) examined the effect of exogenous VIP on changes in vaginal blood flow in women who were either receiving or not receiving hormone replacement therapy. Significant increases in vaginal blood flow were observed only in women receiving hormone replacement therapy, suggesting that estrogen and progestin influence VIP function and, in turn, facilitate vasocongestion. Similarly, animal models indicate that estrogen is critical for NO-dependent smooth muscle relaxation [43], vaginal blood flow [44], and lubrication [45]. In a study conducted by Berman and colleagues, estrogen replacement therapy led to significant increases in NO expression in ovariectomized compared to intact animals [46]. The authors suggested that estrogen may help regulate vaginal NO expression and that NO expression may modulate vaginal blood supply and the relaxation of smooth muscle tissue [c.f. 47].

Hormones

In addition to estrogens, androgens play a critical role in genital blood flow. Aside from serving as precursors to estrogen biosynthesis [48], their vasodilatory effects [49] facilitate blood flow and likely aid in the production of lubrication. Although the precise role of androgens on vaginal blood flow and tissue structure is currently unknown [48], researchers have theorized that androgens and estrogens may interact to facilitate sexual arousal. To examine this, Min and colleagues [45] treated ovariectomized animals with either estradiol or testosterone and measured changes in genital blood flow. Compared to non-ovariectomized animals, significant increases in genital blood flow were found only in those treated with estradiol; treatment of testosterone did not restore genital blood flow. Unfortunately, combination treatments were not examined in this study, though these results corroborate findings presented in Pessina et al. [35] and Witherby et al. [36].

Functional Modulation of Lubrication

Animal models suggest that estrogens and androgens also modulate the production of vaginal lubrication (e.g., [45]). Some direct effects of sex steroid hormones on lubrication have been noted in the literature (for a review, see [50]), though their exact acting mechanisms are unknown. For example, androgens have been found to play a critical role in the glycoprotein synthesis required for vaginal mucification [51], which is characterized by changes in the cells of the epithelium from squamous (i.e., flat) to columnar (i.e., tall), mucus-secreting cells (for a review, see [52]). Thus, a relative androgen deficiency, which could be manifest in low levels of bioavailable androgens, may hinder the production of lubrication.

In addition to androgens, estrogens appear to play a facilitatory role in vaginal lubrication. In a prospective, randomized control trial examining the effects of ethinylestradiol on sexual function in postmenopausal women, Sarrel [53] reported that those treated with ethinylestradiol experienced

improvements in vaginal blood flow and dyspareunia, which refers to difficulty or pain associated with vaginal penetration [54]. However, decreases in vaginal blood flow and increases in dyspareunia were observed when these women were treated with the progestin medroxyprogesterone. Similar beneficial effects of estrogens in combination with androgens on dyspareunia and vaginal lubrication have been reported by others [55]. Estrogens and androgens may therefore mitigate vaginal dryness and dyspareunia, while progestins may blunt these beneficial effects [53, 56]. Taken together, it is likely that interactions between androgens and estrogens yield maximum benefits for healthy vaginal blood flow and lubrication in women.

Measuring Lubrication

Researchers most commonly implement self-report measures of genital lubrication since there is no common objective measurement implemented by researchers [57]. The use of subjective assessments for physiological outcomes such as vaginal dryness is problematic, however, as self-report data does not reliably align with objective indices [58, 59]. Although objective measures (e.g., cotton swabs) are frequently used to assess lubrication in animal models, their application to women has been limited. Early studies of vaginal lubrication in humans primarily assessed the quantity of lubrication during unaroused states using cotton swabs [60], tampons (e.g., [61, 62]), and evaporimeters [63]. Cotton swabs and tampons serve to collect vaginal lubrication, whereas evaporimeters assess humidity within the vagina.

Although cotton swabs and tampons have been more commonly implemented, their use in humans has not been reported in the scientific literature for at least three decades. Tampons and cotton swabs are weighed on a calibrated scale before and after being worn in the vaginal canal for a given length of time, such as 6 [62] to 8 h [61]. Using tampons, Preti and colleagues [62] and Riley and Riley [64] observed substantial increases in lubrication within the vaginal canal following sexual stimulation and orgasm, respectively. However, repeated testing with tampons and cotton swabs is not recommended as their high absorbency and wicking capacities may cause atypical dryness in the vaginal epithelium [8]. Significant increases in vaginal moisture following sexual stimulation have also been detected by an evaporimeter, a device that measures humidity within the vaginal canal [63].

More recently, Carranza-Lira and colleagues [65] implemented a pH test trip placed at the vaginal introitus to examine vaginal dryness unrelated to sexual stimulation or arousal in post-menopausal women. Over a decade later, Dawson, Sawatsky, and Lalumière [66] adapted Carranza-Lira et al.'s methodology specifically to assess genital lubrication in response to sexual films by placing a blue litmus test strip attached to a plastic applicator at the introitus. Significantly greater levels of lubrication were observed after the sexual films in comparison to the nonsexual films, suggesting that litmus strips are sensitive enough to detect lubrication produced in response to sexual arousal specifically. Although litmus strips are suitable for repeated measurement due to their low wicking capacity, they are not without limitations. Firstly, the use of calipers to measure the moisture absorbed by the paper, which is not commonly ruled, introduces an increased risk of measurement error. Additionally, since wicking capacity varies within and between litmus strips depending on whether they are made of plastic or paper (e.g., [67]), inconsistent measurements across clinics and laboratories proves problematic.

To circumvent these limitations, Handy and Meston [68] introduced Schirmer Tear Test strips as an alternative measurement of vaginal lubrication. These strips are approved by the Food and Drug Administration for the clinical assessment of dry eyes and are also commonly used in clinical research examining moisture produced by mucous membranes such as the eyes (e.g., [69]), nose (e.g., [70]), and mouth (e.g., [71]). The strips are designed to measure moisture production using grade 41 quantitative filter paper, a type of ashless filter paper that facilitates fast and consistent wicking throughout the test strip. Additionally, the strips are ruled in millimeters which alleviates the need for calipers or other measurement devices and may facilitate more accurate interrater reliability. Women with ($N=32$) and without ($N=32$) sexual arousal difficulties demonstrated significant increases in vaginal lubrication in response to viewing a sexual film; however, no between-group differences were observed for pre- or post-film levels of lubrication [68]. Moderate correlations were found between physiological lubrication and perceived genital arousal ($r=0.41$) and lubrication ($r=0.30$); similar correlations between physiological lubrication and perceived genital arousal were previously reported by Dawson et al. (0.51) [66] and Sawatsky et al. (0.37) [72] with litmus test strips. Although Handy and Meston's findings provided preliminary support for the use of Schirmer Tear Test strips in measuring vaginal lubrication, further research is required to determine the psychometric properties of this application.

Conclusion

During sexual arousal, increased blood flow to the genitals causes a localized increase in pressure, thereby allowing plasma transudate to pass through the vaginal walls and collect on the vaginal surface. The production of lubrication

is an integral component of the female sexual arousal response as it primes the vaginal canal for penetration and may enhance sexual pleasure. In addition to supporting healthy vaginal tissue structure and blood supply, sex steroid hormones appear to have beneficial downstream effects on vaginal lubrication, although their exact mechanisms of action have yet to be determined. Self-report measures of vaginal lubrication have prevailed over the use of tampons and cotton swabs in the recent literature. However, preliminary support has emerged for the use of litmus strips and Schirmer Tear Test strips as safe, accurate, and objective measures of lubrication.

Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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