



Southern California Center for
SEXUAL HEALTH
and SURVIVORSHIP MEDICINE

Brave New World of Moisturizers and Lubricants

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Disclosures: **Speakers Bureau** Scynexis

Consultant /Advisory Board Viveve Medical, Materna, Exeltis, Synexsis, Innovus, Dare pharmaceutical

Objectives

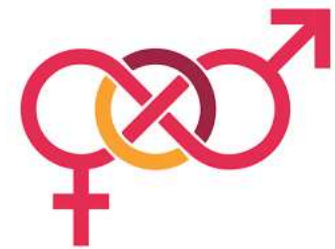
- After the presentation, the participant will be able to
 - Identify common causes of GSM/VVA
 - Identify medications that can contribute to vaginal dryness
 - Discuss non hormonal treatment options that may help treat the symptoms of GSM/VVA

DISCLAIMER:

Brand names maybe mentioned in this talk

This is NOT an endorsement of any specific product by the speaker or the conference

I will typically discuss sexual health from a cis-female and cis-male perspective (using gendered terms and pronouns) due to convention. However, the sexual health needs of all genders are important and relevant.



Unmet need

- 157 million women in the USA
- 41% are postmenopausal
- 64 million postmenopausal women
- 34 million atrophic women
- 40% of life in the post menopause
- Only 7% receive prescription treatment
 - 2.3 million treated women



"You're painfully dry?"

Goals of Treatment

- Relieve symptoms
- Reverse anatomical changes
- Improve sexual function and quality of life

Lubricants and Moisturizers

- Lubricants are considered temporary measures to relieve vaginal dryness during intercourse
 - Short duration of action
 - Must be applied frequently
 - Sexual aid
- Moisturizers are promoted as providing long-term relief of vaginal dryness
 - Continuous use- several times a week
 - Everyday aid
- Both OTC and FDA approved as cosmetics
- **510K clearance is the new normal**

● **Moisturizer = Maintenance**

● **Lubricant = Love making**

Lubricants are not just for Dry Old Women!

- Sexual Pleasure
- Medications
 - Oral contraceptives
 - Anti histamines
- Partner issues
 - PD5 Penis/ Menopause and andropause
 - Ignorant lover syndrome
 - Delayed ejaculation
- Dryness through the Lifecycle
 - Lactational Amenorrhea
 - Chronic Medical Conditions
 - Breast Cancer
 - Hickey et al (2016)
 - Menopause



5 Classes of Lubricants

- **LTZ (Class II Medical Device) – Condom With Nonoxynol-9. Regulation# 884.5310**
FDA Link: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=3666>
- **KMJ (Class I Medical Device) – Lubricant, Patient. Regulation# 884.6375**
FDA Link: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=2422>
- **NUC (Class II Medical Device) – Lubricant, Personal. Regulation# 884.5300**
FDA Link: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=3697>
- **PEB (Class II Medical Device) – Lubricant, Personal, Gamete, Fertilization, and Embryo Compatible. Regulation# 884.5300**
FDA Link: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=3727>
- **MMS (Class I Medical Device) – Lubricant, Vaginal, Patient. Regulation# 880.6375**
FDA Link: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?ID=2476>

- The FDA 510(k) Clearance Overview states
 - “Specifically, medical device manufacturers are required to submit a premarket notification if they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected.”
- That means in order to sell a personal lubricant to consumers, a company must notify the FDA of its intent to manufacture and sell the product as well as making sure the ingredients will not harm people.
- **You would be surprised if you knew just how many lubricants are being sold with having gone through this required testing.**
- 510(k) Database
Link: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm>

Is Your Lubricant 510K Cleared

- YES

- Uberlube
- Wet Platinum
- Good clean love
- Astroglide Natural
- Preseed
- Swiss Navy II natural
- Yes Water based
- Organic Glide

- NO

- Slippery Stuff
- Sliquid Natural Water
- Dreambrands the natural
- CocoNu
- Intimate earth hydra
- Nooky lube

Lubricants

- Duration: short or long acting
- Age: all ages
- Use:
 - Pleasure enhancement
 - Sexual aid: Minimize friction and irritation around the clitoris, labia and vaginal entrance and both partners' genitals
- Consistencies: Gel or liquid
- Forms: water-based, oil-based, silicone
- Ingredients: many perfumes, flavors or warming components

Lubricant Use and Pleasure

Association of Lubricant Use with Women's Sexual Pleasure, Sexual Satisfaction and Genital Symptoms: A Prospective Daily Diary Study N=2,453 \geq 18 YRS.

Assigned to 1 (of 6) water or silicone based

*Use of Lubricants associated with significant higher

**REPORTS OF
SEXUAL PLEASURE AND SATISFACTION**



Durex Global Sex Survey: 41 countries/ N=317,000 / 138 x /yr

Enhancement Statistics

- 43% use vibrators
- **59% lubricants / moisturizers**
- 53% pornography
- 13% penis rings
- 5% penis sleeves
- 6% loveballs
- 35% pleasure enhancing condoms
- **43% massage oils**
- 26 % erotic literature

“What do Women Want..”

- Ease of use, long-lasting
- Safe for skin
- Not messy, no residue, no taste, no color
- Consistency similar to vaginal secretions
- Moisture to decrease effects of medications
- Irritant free
- Natural additive free: Organic, nontoxic, “green”
- Pleasure enhancing; orgasm enhancing
- Non hormonal or minimally locally absorbed
 - (if hormonal)

What do Men want

- Most men have used a lubricant
- Most common use is for intercourse, next was solo masturbation
- Use is common across all ages
- Primarily for
 - Sexual enhancement
 - Comfort
 - Pleasure
 - Curiosity
 - My partner wanted to

Reece et al (2014) J Sex Med. National Survey of Health and Behavior

Water Based Lubricant



Advantages

- inexpensive
- available
- toy compatible
- condom compatible
- easily washes off
- Breast Cancer
 - Hickey et al (2016)

Disadvantages

- sticky
- short acting
- many have preservatives (irritation and infection)



Silicone Lubricants

Advantages

- no taste
- no smell
- no impact on osmolality
- more slippery
- lasts longer
- less irritating
- no glycerin
- condom compatible
- anhydrous –no effect on ph
- Breast Cancer
 - Hickey et al (2016)

Disadvantages

- expensive
- not as readily available
- not silicone toy compatible
- can stain sheets



“Specialty” Lubes

- Flavored Water Based Lubes
 - -edible
 - Silicone based
- Warming Lubes
 - capsaicin



Who Needs Moisturizers?

- **Vaginal Moisturizers**

- provide long-term relief of vaginal dryness independent of coitus

- **Dryness Suffers:**

- **Estrogen deficiency**

- Menopause, breastfeeding, oophorectomy, medications

- **Medications**

- Anticholinergic, antihistamines, TCA

- **Chemical sensitivities**

- Douches, soaps

- **Pelvic radiation**

- Loss of small blood vessels and direct damage to the vaginal mucosa

Vaginal Moisturizers

- Moisturizers are Not lubricants, but lubricating
- 2 times/week
- Increase water content in vagina
- Also useful in women as a “supplement” to vaginal estrogen or lubricants

Osmolality Of Lubricants

- Vaginal secretion OSM: 260-370 mOsm/kg
- Semen 250-380 mOsm/kg
- High concentration of glycerol, propylene glycol, and other compounds-lubricants 4-30 times osmolality of the vaginal fluid
- Hyperosmolar lubricants
 - Marked toxicity to human colorectal epithelia in vivo
 - Increase vaginal transmission of Herpes in mouse models
 - Increase susceptibility to HIV in target cells in cell culture
- Lubricants varies composition, unphysiological pH, osmolality & additives
- Higher osmolality the higher potential to cause irritation of the mucosa, cellular, tissue damage and affects sperm motility
- When hyperosmolar lubricants placed directly to the rectum in humans, it caused significant damage and denudation of the epithelium
- Consistent reports of safety concerns regarding hyperosmolar lubricants

Potter et al (2021) Climacteric; D Edwards (2016) Climacteric ; Ayehunie et al (2017) Toxicology Reports

Introduction

- Over 6000 individuals enter the menopause each day in the USA and 50% of them suffer from GSM.
- Vaginal dryness maybe associated with hypoestrogenic postmenopausal individuals.
- It may also occur due to chronic medical conditions and as a direct side effect from medications. There are over 300 medications that can cause vaginal dryness.
- Over the counter personal lubricants can address sexual complaints and symptomatology associated with vaginal dryness, although clinically published data supporting their efficacy remains limited.
- While personal lubricants may alleviate symptoms, their definitive effects on the vaginal microbiome remain understudied and underappreciated

- Osmolality refers to a substance's ability to draw moisture out of tissues and cells. Exposure to a lubricant with a higher osmolality than normal vaginal secretions can result in vaginal tissue which shrivels up because the moisture in those cells is pulled out.
- This process leads to irritation and a breakdown of the mucous membrane barrier which protects the vagina from infection.
- Disrupted vaginal mucous membranes have been associated not only with irritation and discomfort but also with increased risks of sexually transmitted infections such as HIV.
- Unfortunately, many currently marketed lubricants have high osmolalities which are detrimental to vaginal tissue

- In order for a personal lubricant to be sold and marketed in the United States, the FDA has started requiring all lubricants to have a Class II Medical Device 510(k) clearance
- The WHO recommends using a lubricant with a pH of 4.5 and an osmolality below 1200 mOsm/kg.
- Age-associated vaginal-physiological changes due to a hypoestrogenic milieu include increased pH, decreased natural lubrication, reduced endothelial rugae and impact on the vaginal microbiome.
- Little is known about how personal lubricants may impact the vulvovaginal microbiome.



Product	Ph	Osmolality (mOsm/kg)
KY Jelly	3.5 +/- 0.2	3,631 +/- 13
Rephresh	3.4 +/- 0.1	1.439 +/-6
Replens	3.0 +/- 0.1	1177 +/-5
Sylk ®	4.4-4.7	688-696

Acceptable limit @ 600-1077 mOsm/kg

Ideally: WHO should not exceed 380 mOsm/kg (2021)

Now: WHO recommends no greater than 1200 mOsm; pH 4.5

**Most products do not comply with pH and osmolality
Recommended standards (2000-6000 mOsm/kg)**

A randomised trial on the effectiveness of five water-based personal lubricants in premenopausal and postmenopausal individuals

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Study Objectives



Primary objective

- To establish the effectiveness of five personal lubricants in pre- and post-menopausal individuals who experience intimate discomfort associated with vaginal dryness



Primary endpoint

- Change from baseline in total Female Sexual Function Index (FSFI) score at 4 weeks post lubricant use

Secondary endpoint

- Change from baseline in the FSFI individual domain scores (desire, arousal, lubrication, orgasm, satisfaction, and pain) at 4 weeks post lubricant use



Safety objective

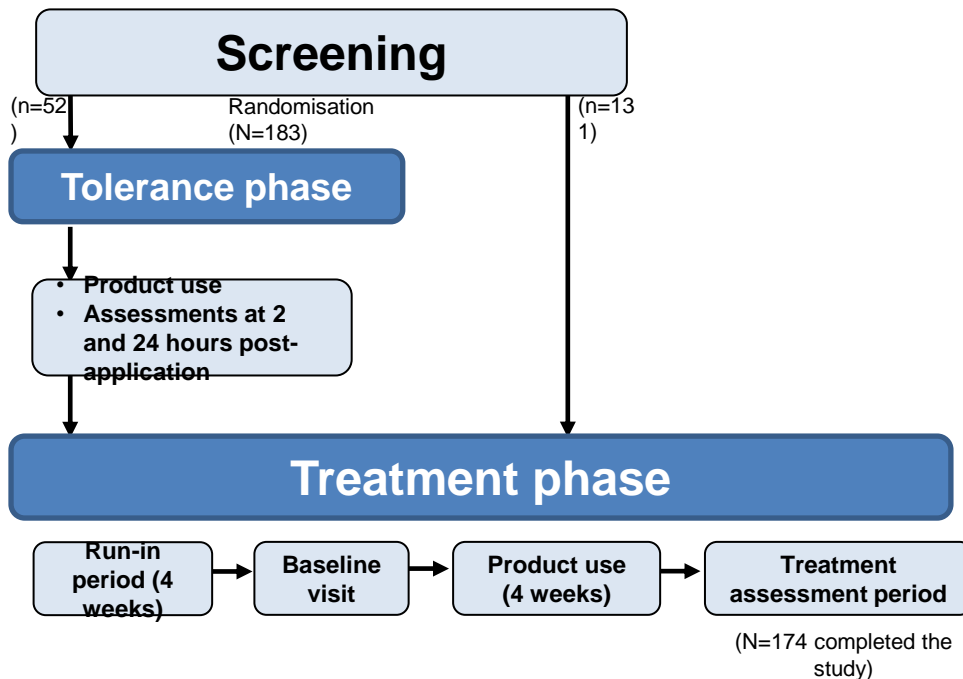
- To assess the safety of the five personal lubricants in women who experience intimate discomfort associated with vaginal dryness



Success criteria

- An increase of 4 points in the FSFI score from baseline to 4 weeks post lubricant use is considered a clinically important change

An Open-Label, Five-Arm, Parallel Study Design

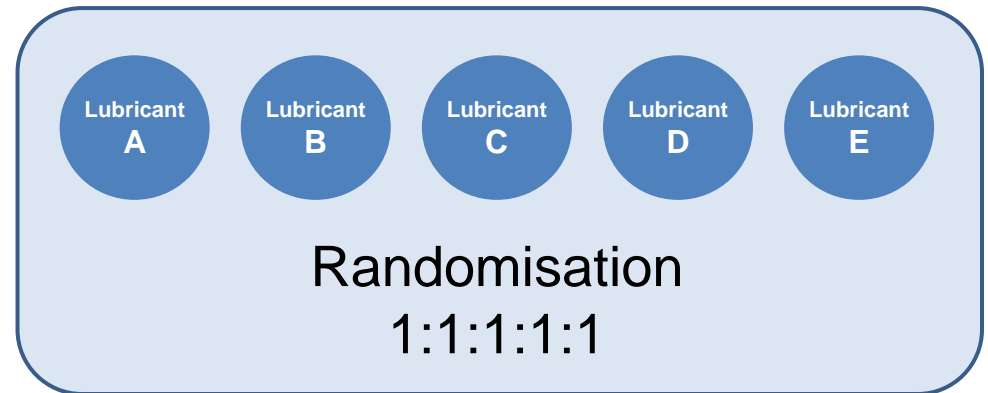


Study population

- Subjects in a mutually monogamous heterosexual relationship ≥ 3 months
- Sexually active (having sexual intercourse at least once a week)
- Experience discomfort during vaginal penetrative sex
- Mild to moderate vaginal dryness and dyspareunia on Verbal Rating Scale (VRS)
- Pre- and post-menopausal individuals (approx. 50:50 ratio for both tolerance and treatment phase per product)

Methodology

- Participants were randomised to one of five lubricants, stratified by menopausal status (pre- or post-menopausal)
- Subjects were shown how to apply personal lubrication to the vagina and vulva
- The allocated lubricant was used at least once a week over a 4-week period for penile/vaginal intercourse
- Weight of lubricant was recorded when dispensed and again when subjects returned at the end of the 4-week use



The Personal Lubricants Studied

- Personal water-based lubricants compatible with natural rubber latex and polyisoprene condoms
- Four lubricants (B-E) have been reformulated to meet the WHO osmolality guideline of $\leq 1,200$ mOsm/kg
- Fifth lubricant (A) was well-established hyperosmolar included as a control

Lubricant	pH	Osmolality (mOsm/kg)
Lubricant A	5.1–5.8	5136
Lubricant B	3.5–4.5	663–1063
Lubricant C	3.5–4.5	850–1200
Lubricant D	3.5–4.5	780–1180
Lubricant E	3.5–4.5	780–1180

Study Assessments

Tolerance phase	Treatment phase
Vaginal epithelial tolerability (VET) assessment	Female Sexual Function Index (FSFI) A validated, 19-item self-report questionnaire which measures sexual functioning in women, including: <ul style="list-style-type: none"> • Sexual desire • Sexual arousal • Lubrication • Orgasm • Satisfaction • Pain
Vaginal hygrometer	
Vaginal pH	Subject diary
Global assessment of tolerance	Global evaluation of product effectiveness, tolerability and usability
Overall tolerance rating statement	Adverse events
Microbiological swab of vagina	
Subject perceived questionnaire (SPQ)	

An increase of >4 points in the total FSFI score was observed for all five lubricants after 4 weeks

Lubricant	n	Mean baseline score	Mean change from baseline	Median change from baseline (99% CI)	p-value*
Lubricant A	35	24.02	5.19	5.20 (3.00, 7.25)	<0.0001
Lubricant B	32	23.32	7.11	6.45 (4.55, 9.05)	<0.0001
Lubricant C	35	23.74	5.44	5.50 (3.70, 7.30)	<0.0001
Lubricant D	36	23.87	5.13	4.73 (2.90, 6.80)	<0.0001
Lubricant E	36	23.14	5.66	5.67 (3.60, 7.55)	<0.0001

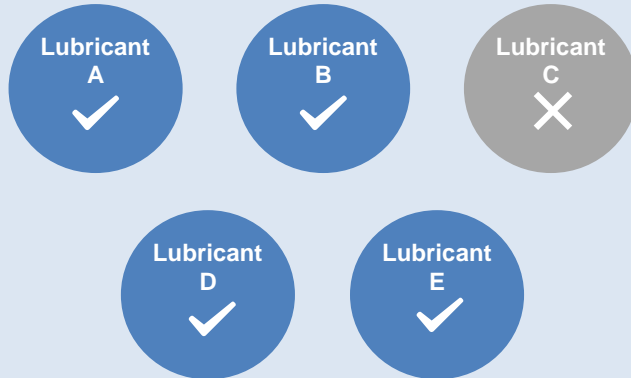
A **significant** improvement was also seen across all six domains of the FSFI from baseline to 4 weeks of use with all five lubricants (p<0.0001 for lubrication and pain reduction and p<0.05 for all other domains)



Clinically Meaningful Improvements in FSFI were seen in both Pre- and Post-Menopausal Individuals

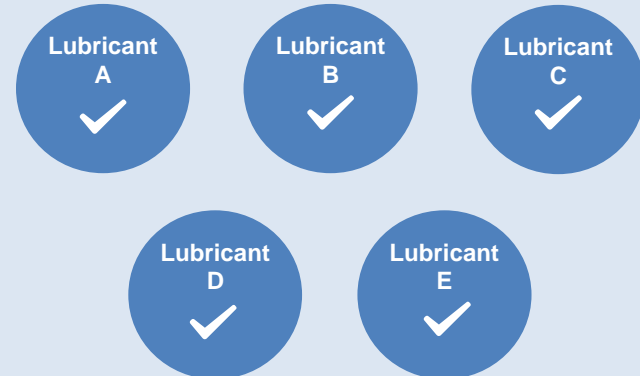
Pre-menopausal

4/5 lubricants showed an increase in FSFI score of >4 points, as indicated by the mean differences from baseline



Post-menopausal

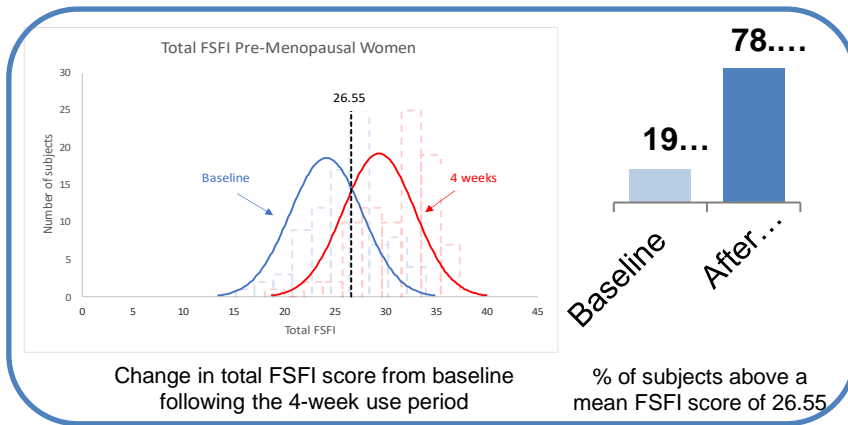
All lubricants showed an increase in FSFI score of >4 points, as indicated by the mean differences from baseline



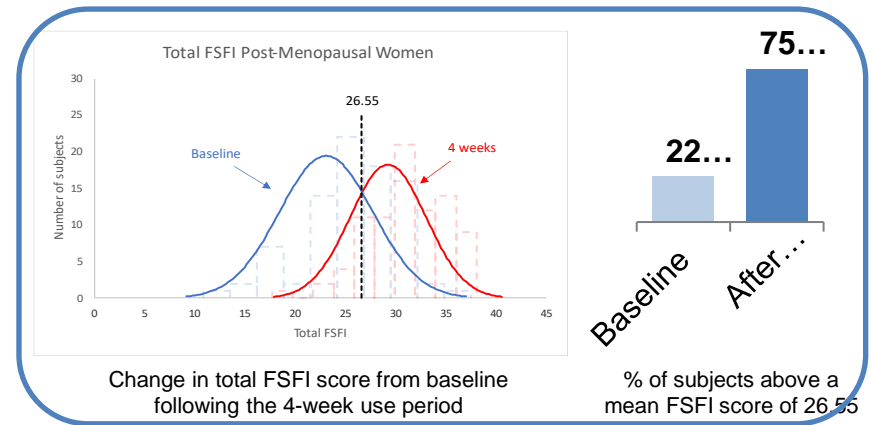
A Total FSFI Score of >26.55 is Indicative of Normal Sexual Function

Following treatment, the number of subjects with sexual function (mean FSFI >26.55) was **significantly greater** than the number with sexual function prior to treatment for both subgroups ($p < 0.0001$)

Pre-menopausal



Post-menopausal



Secondary Ad hoc Analysis

Examined if these newer lubricants influenced the vaginal microbiome of individuals from different age groups.

Top Line Results: Vaginal Biome

- Repeated lubricant application did not significantly alter the vaginal microbiome for up to 4 weeks post-product application.
- Microbial diversity and relative abundance differed significantly between age groups but remained unaffected during product application.
- Relative abundance of Lactobacilli negatively correlated with vaginal pH.
- Gardnerella showed a positive correlation with vaginal pH across all age groups
- Non-parametric ordination methods and multivariate analysis of variance showed that repeated application of all lubricants tested, **did not significantly** alter the vaginal microbiome for up to 4 weeks after product application
- Microbiome diversity and relative abundance differed significantly between pre- and post-menopausal individuals but remained unchanged before and after lubricant application

Human Studies

- BV study: 39 women self collected vaginal swabs and data was combined with a behavioral diary
 - Result: BV was linked to lubricant use
- Rectal Study: 380 men, women in LA and Baltimore with any lubricant
 - Result: rSTI are more common with lubricant user.
 - Lubricants appear to modulate vaginal and rectal flora
- Not all glycerin- free lube are the same
- Mucosal tissue toxicity and acute inflammation were noted after lubricant use
- **While current data does not suggest an increased risk for HIV, there is an epidemiological association with BV acquisition and incident STI**
- Studies are difficult to design, small numbers and need confirmation
- **Data is limited but suggests that silicone-based lubricants are safe**

Household Products that should NOT be used with Latex Condoms

- Baby Oil
- Burn Ointment
- Dairy Butter
- Palm Oil
- Coconut Oil
- Cooking Oil
- Fish Oil
- Mineral Oil
- Suntan Oil
- Hemorrhoid cream
- Petroleum Jelly
 - Vaseline
- Body Lotion
- Hand Lotion

Watch for Irritating Ingredients

Benzyl Alcohol

- Maybe drying agent
- Maybe irritant for some women with severe atrophy
- Consider avoidance in vulvodynia patients

Favola et al (2008).
Cosmetic & Toiletries

Glycerin

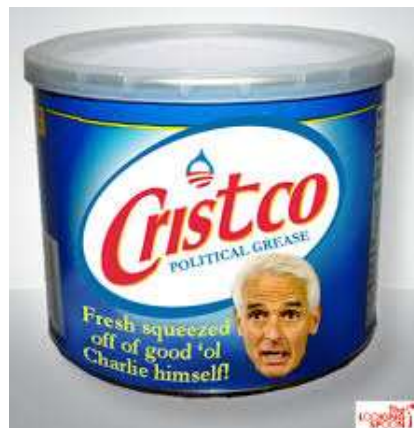
- Can be considered a drying agent
- May be associated with yeast infections
- May upset balance of vaginal flora

Some things are best in a salad and **NOT in your vagina**



Some oil may predispose
To Candida and
Bacterial vaginosis
Infections

Brown JM et al (2013)



“Orzo not Orifice”
Schover L.

Treating your Vagina with respect NO Chemicals

NO
Additives
Parabens
Glycerin
More Regulation



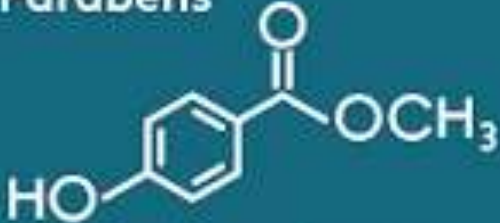
NONOXYNOL-9



(Nonylphenoxypolyethoxyethanol)



Parabens



Parabens are a group of synthetic compounds commonly used as preservatives in a wide range of health, beauty and personal care products.



Vulvar Contact Dermatitis

■ Suspect via history:

- Sudden onset
- Intense pruritus
- Vesiculation
- Weeping lesions

■ Common vulvar irritants

- Spermicides, Bactericides

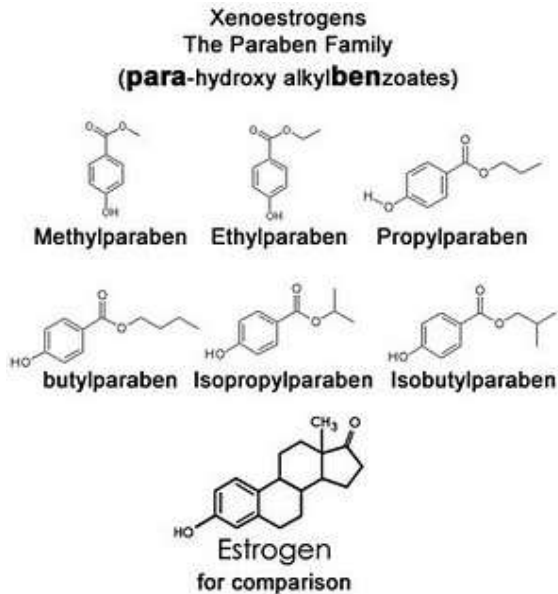
■ Common vulvar allergens

- Benzocaine
- Chlorhexidine (KY jelly)
- Parabens and propylene glycol
- Latex
- Lanolin

Treatment

- Stop all irritants
- Stop overzealous hygiene
- Topical steroids (low potency)
 - daily for 5-7 days
- Bland emollients
 - A&D, mineral oil
- Sleep aid for sedation
avoid scratching
- Antibiotics prn infections

What is a Paraben?



A preservative commonly added to cosmetics, moisturizers and lubricants known for to have antibacterial and antifungal properties

Berger et al: adolescent girls who wear make up daily had a 20 fold increase in propyl-parben in their urine compared to those who rarely wear make up.

Parabens are weakly estrogenic

- US FDA 2005 “
 - Parabens in the concentrations found in cosmetics and other dermatologic products (up to 25%, but typically 1%) pose no logical risk to the consumer”
- American Cancer Society 2008:
 - “insufficient scientific evidence to support that cosmetics increase breast cancer- larger studies are needed
 - RE: parabens and breast cancer risk”

Lubricants and Condoms

- Water and glycol based personal lubricants are generally accepted as being compatible with natural rubber latex and safe with latex condoms
- **Latex Condom integrity and efficacy is compromised by oil-based lubricants:**
 - Baby oil: greatest negative impact on condom strength
60 seconds exposure to mineral oil caused 90% decrease in condoms' strength
Voeller, Contraception 1989;39 : 95-102Rosen, South med J 1999;92:305-7
 - K-Y Jelly and Lubrin do not affect condom strength
Rosen, South med J 1999; 92:305-7
- **Anal Sex – breakage 3% for water-based lubricant versus 21.4 % with no additional lubricant supplied**
 - WHO advisory Note
- Lubricants can increase the risk of condom slippage during vaginal sex
Smith, Int J STD AIDS 1998;9:330-5

Lubricants and Sperm

- Lubricants may affect sperm
 - Integrity
 - function

thereby decreasing
fertilization potential

Lubricants and Sperm

- **Motility is significantly decreased by saliva, olive oil and KY jelly, but not by baby oil**
 - Saliva: 50% in 5 min, 5% in 15 min
 - KY jelly: 26% in 30 min
 - Olive oil: 58% in 15 min, 9% in 30 min
 - Anderson, Hum Reprod, 1998;13:3351-6
- **Motility is significantly decreased by FemGlide (“Slippery Stuff”), Replens and Astroglide but not by Pre-Seed.**
 - Agarwal, Fertil Steril 2008;89:375-379
- **Sperm chromatin integrity is significantly decreased by KY-jelly and FemGlide, but not by Pre-Seed**

Sperm Motility

Most Lubricants Decrease Sperm Motility

Astroglide
K-Y Jelly
Lubrin
H-R Jelly
Surgilube
Touch
Glycerin
Petroleum jelly
Saliva
Replens
Olive oil and vegetable oils

Minimal Effect on Motility

- Canola oil
- Baby oil
- Pre-seed



Dry Sex

- Leiblum et al, 2009, JSM 6;2425-33.
- Preference for “ wet or dry sex” related to cultural norms and couple preferences
- Cloth, paper, cotton wool used as drying agents intravaginally prior to sex
- Areas of South Africa /Brazil dry sex is norm
 - US: “Liquid Virgin” gaining popularity
 -



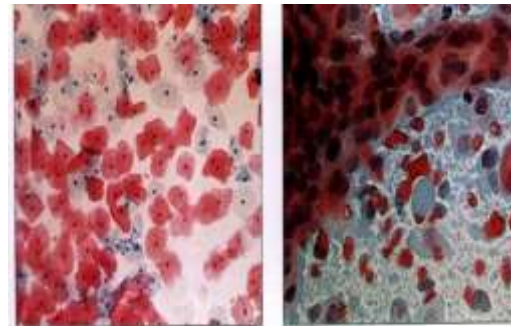
When Lubricants & Moisturizers are Not Enough..

Moderate to Severe GSM:

- *BURNING
- *DRYNESS
- *ITCHING
- *RAWNESS
- *PAIN
- *THIN, PALE, FRAGILE EPITHELIUM
- *DECREASED SUBCUTANEOUS FAT
- *PATCHY ERYTHEMA
- *INCREASES FRIABILITY
- *DYSpareunia

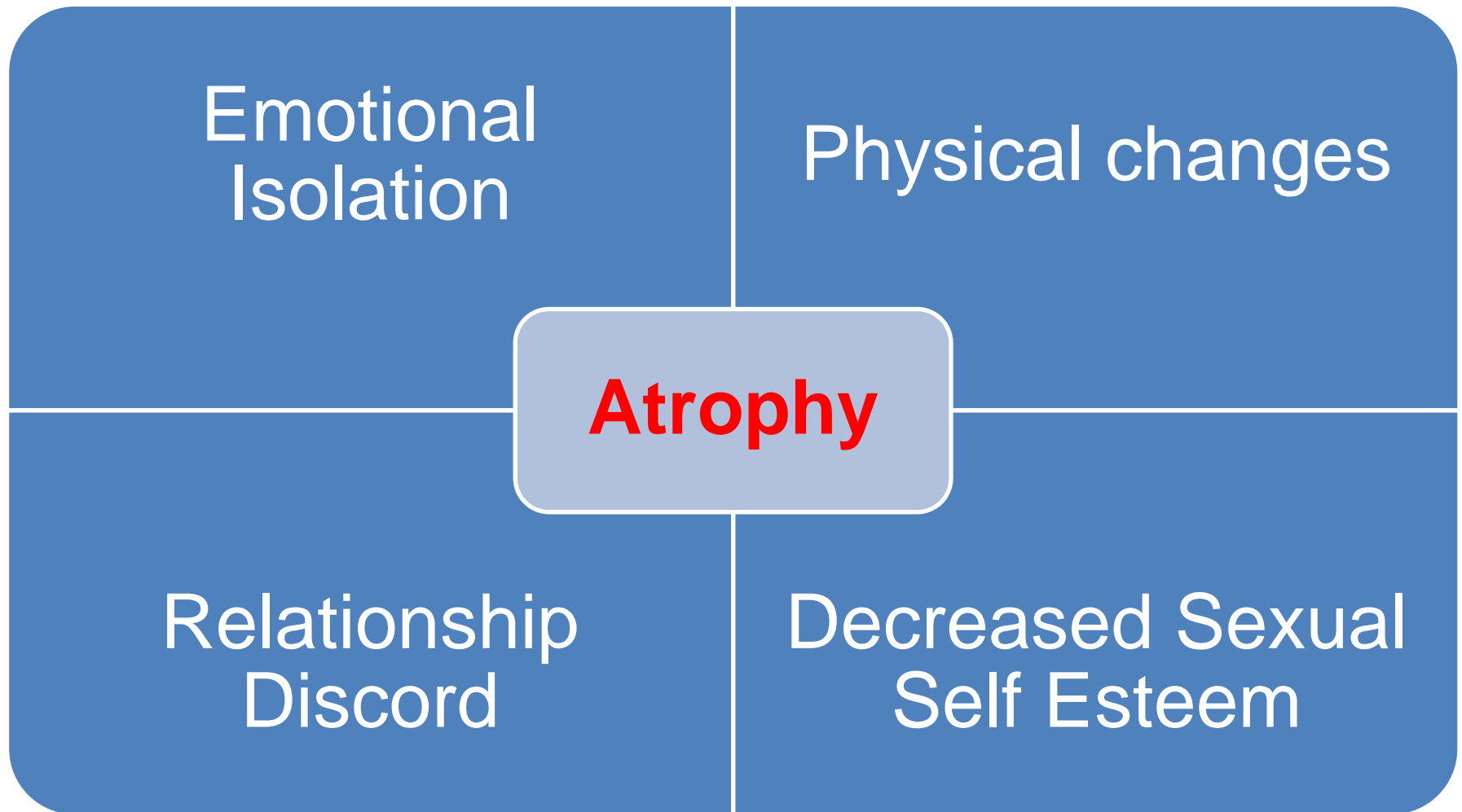


Medscape



*SYMPTOMS DO NOT ABATE AND OFTEN PROGRESS OVER TIME

The Impact of Atrophy



Important References

- Global Consultation on Personal Lubricants (2016)
- Brown et al (2016) Motivation for intravaginal product use among a cohort of women in Los Angeles . PLOS.
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- Blair et al (2020) Lubricants and Rectal Douching. Int J STD AIDS.
- Jozkowski et al (2013) Women's Perception about Lubricant Use and Vaginal Wetness During Sexual Activity. JSM
- Environmental Health Perspectives Volume 122 Number 3: March 2014