Beyond Estrogen: Exploring Regenerative Approaches in Genitourinary Syndrome of Menopause

A review of mechanisms, current evidence and clinical considerations

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April 9, 2026

Learning Objectives

At the end of the program, participants will:

- Describe the relevant anatomy of the female vulvovaginal and lower urinary tract and the physiologic changes that occur during menopause
- Describe the clinical features of genitourinary syndrome of menopause (GSM), including commonly used assessment tools and current standard treatments
- List the potential mechanisms of platelet-rich plasma (PRP) and it’s potential role as an adjunctive therapy in the management GSM

Disclosures of Affiliations, Financial Support and Mitigating Bias

- Speaker Name: Dr. Kersti Kents
- Session title: Beyond Estrogen: Exploring Regenerative Approaches in Genitourinary Syndrome of Menopause
- I have no relationships with for-profit or not-for-profit organizations
- I can confirm that I had full editorial control of the content of this presentation
- All treatments discussed are consistent with the approved Canadian Product Monogragh

Barriers to Care

- What barriers do you foresee when assisting women with signs and symptoms of GSM?

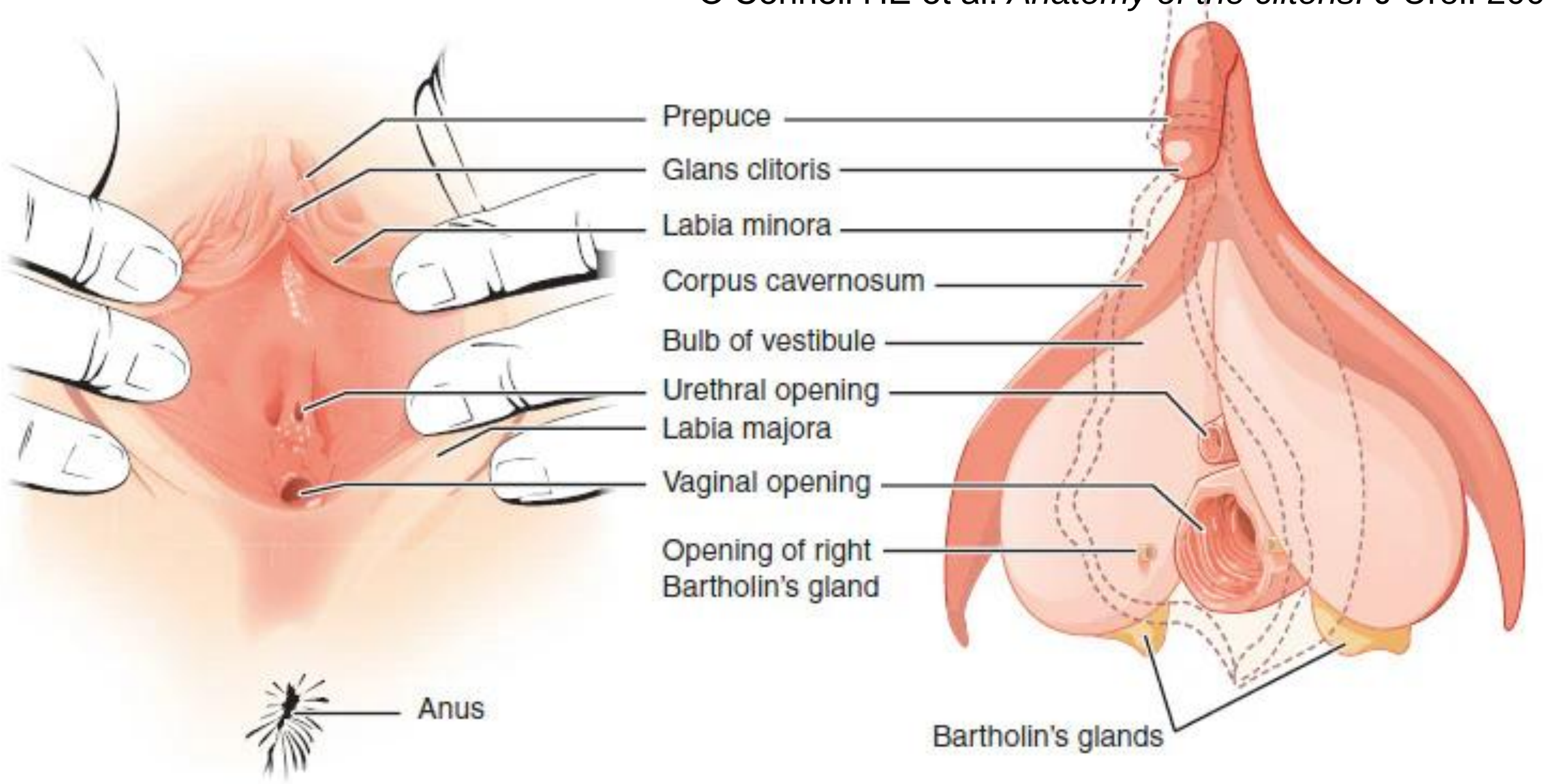
Still Discovering Women’s Health

In 1969, we put a man on the moon.
In 1982, we developed the internet.
In 1998, we discovered the full anatomy of the clitoris.

— Helen O’Connell

Women’s health has historically been underrepresented in research — and many areas, including GSM, are only now gaining focused attention.

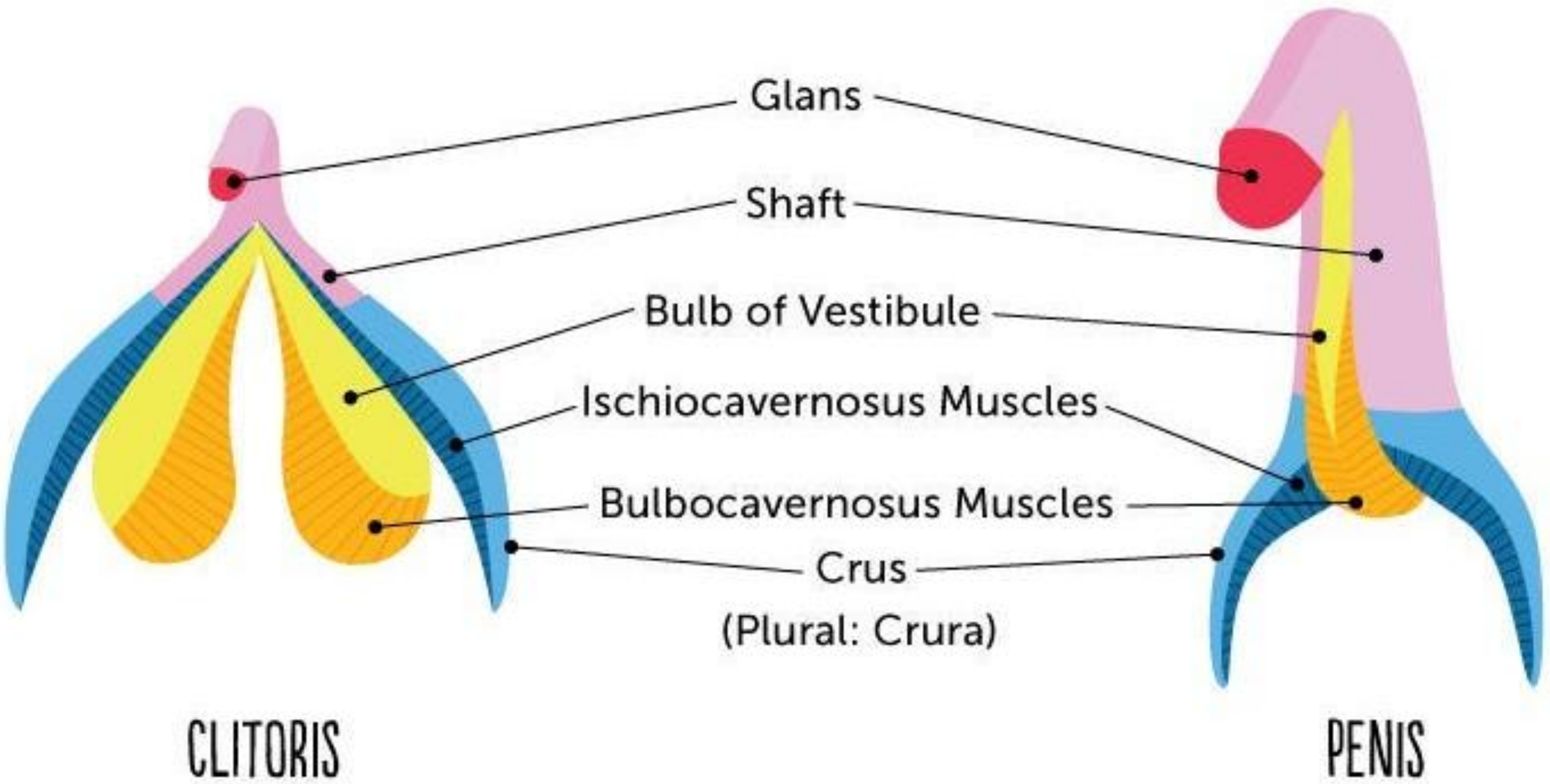
O'Connell HE et al. *Anatomy of the clitoris.* J Urol. 2005



Vulva: External anterior view

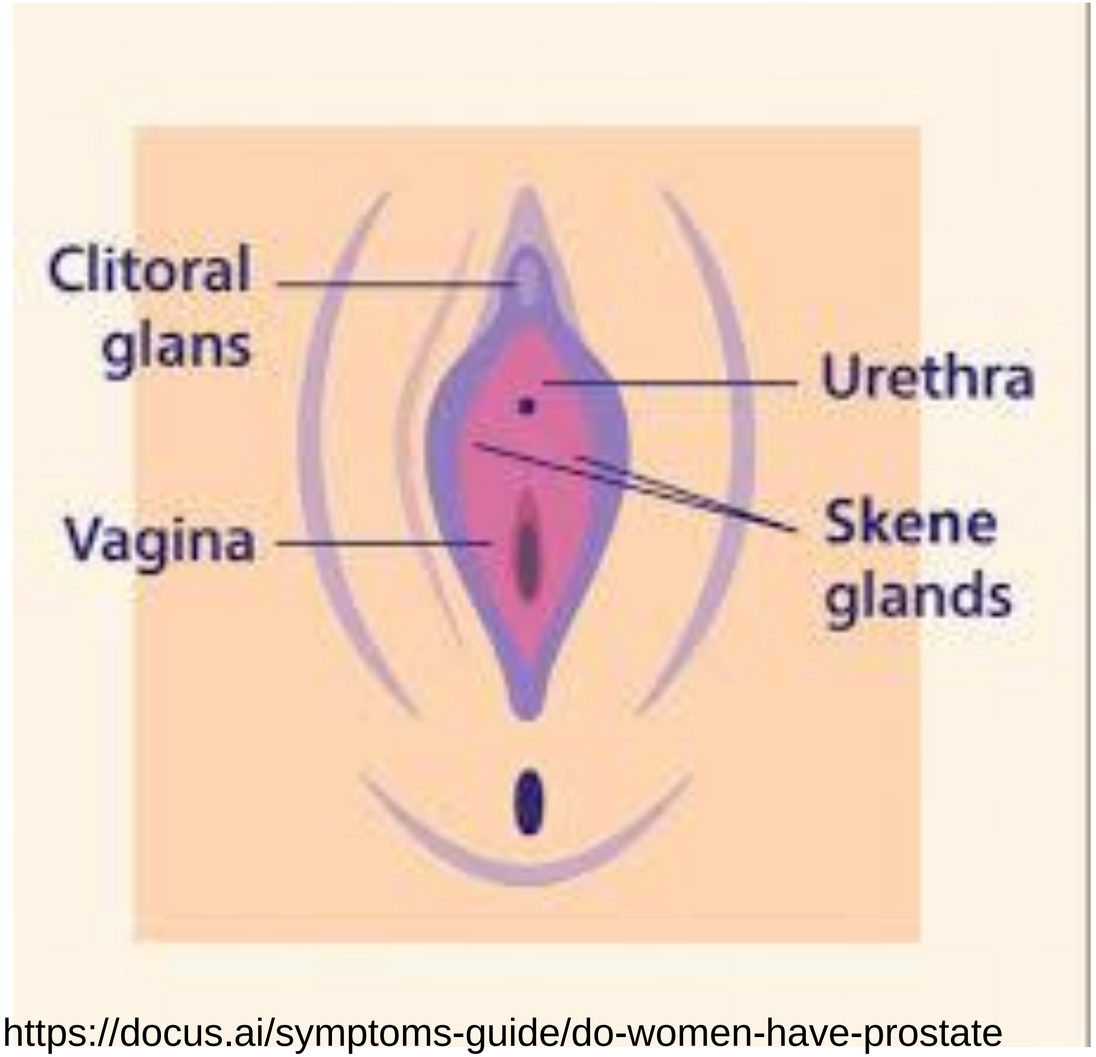
Vulva: Internal anteriolateral view

HOMOLOGOUS STRUCTURES IN THE CLITORIS AND PENIS



https://carlynbeccia.substack.com/p/8-fun-facts-about-the-female-erection

Skene Glands and G Spot



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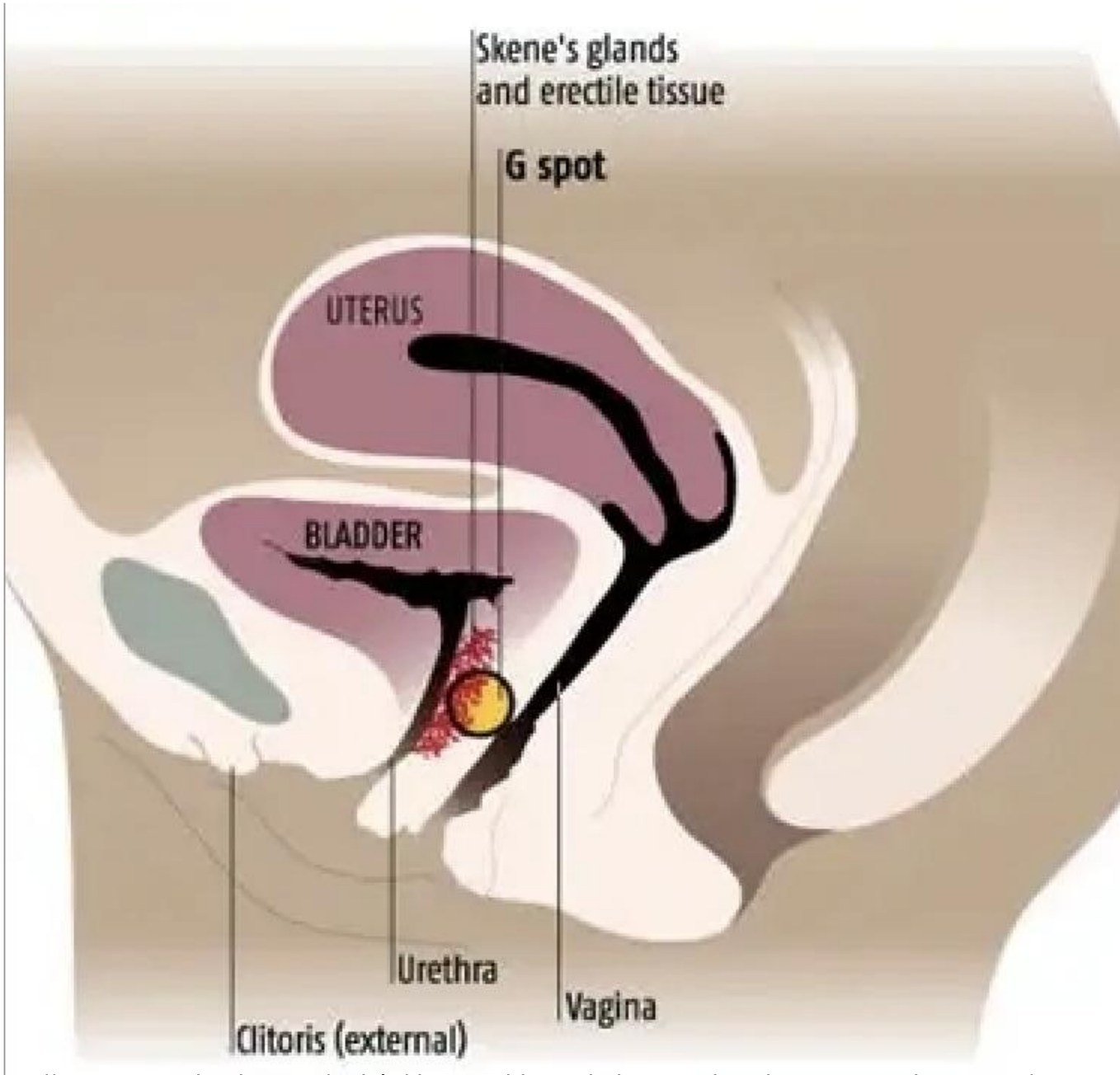
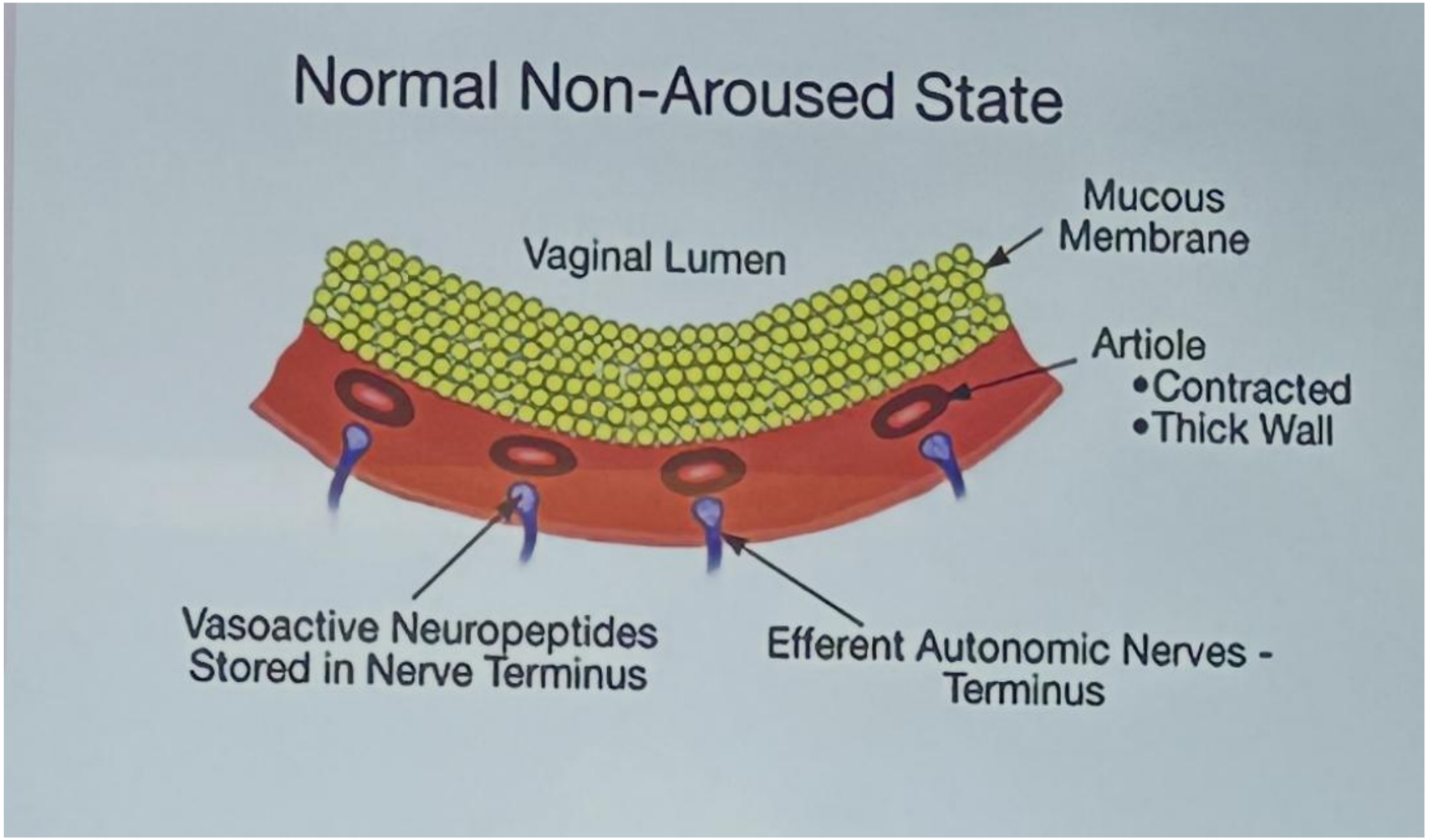


https://www.newscientist.com/article/dn2495-bigger-is-better-when-it-comes-to-the-g-spot/

Vaginal Lubrication

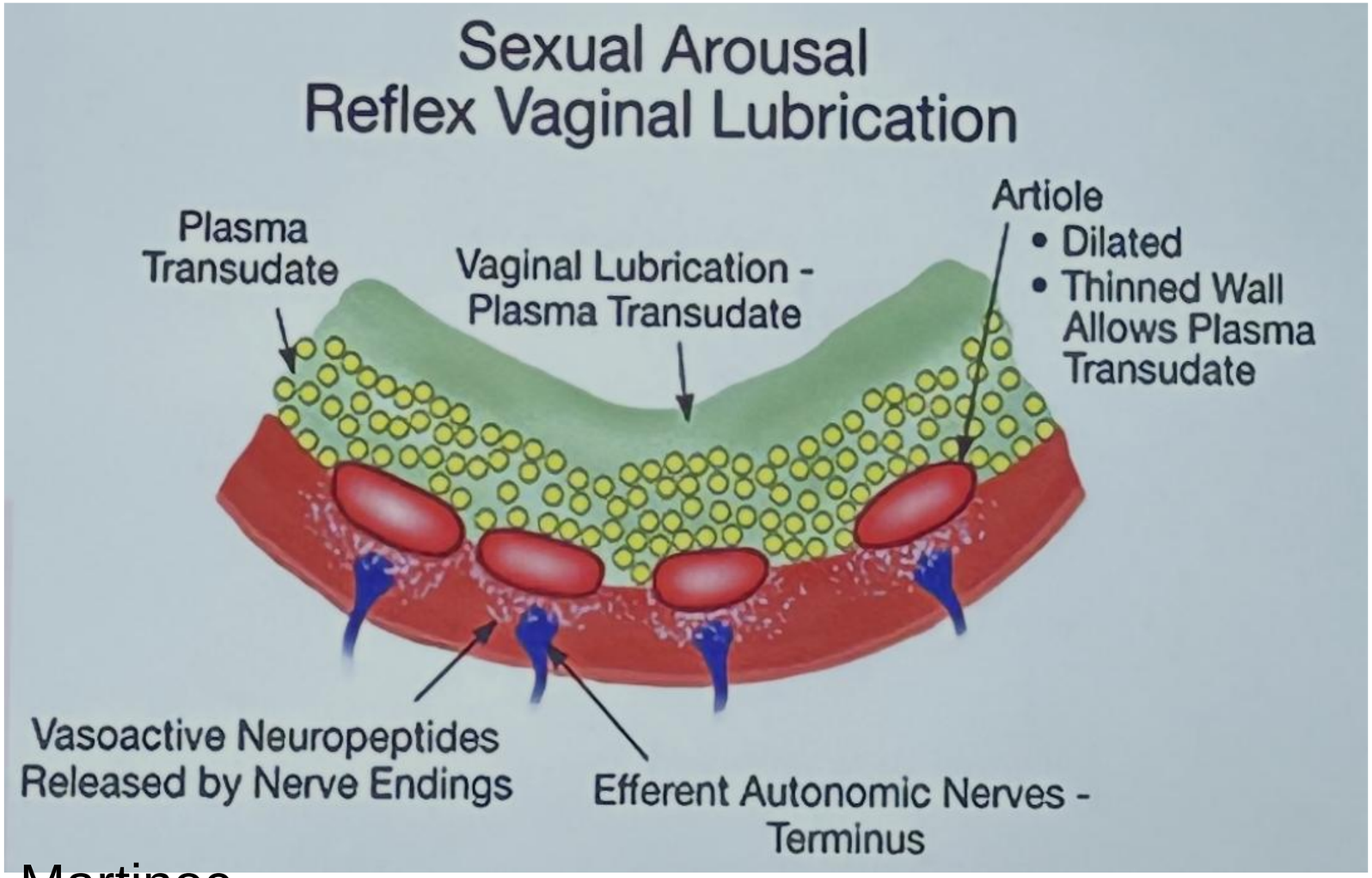
Normal Non-Aroused State



C/O Dr. Ksenija Martinec

Vaginal Lubrication

Sexual Arousal - Reflex Vaginal Lubrication



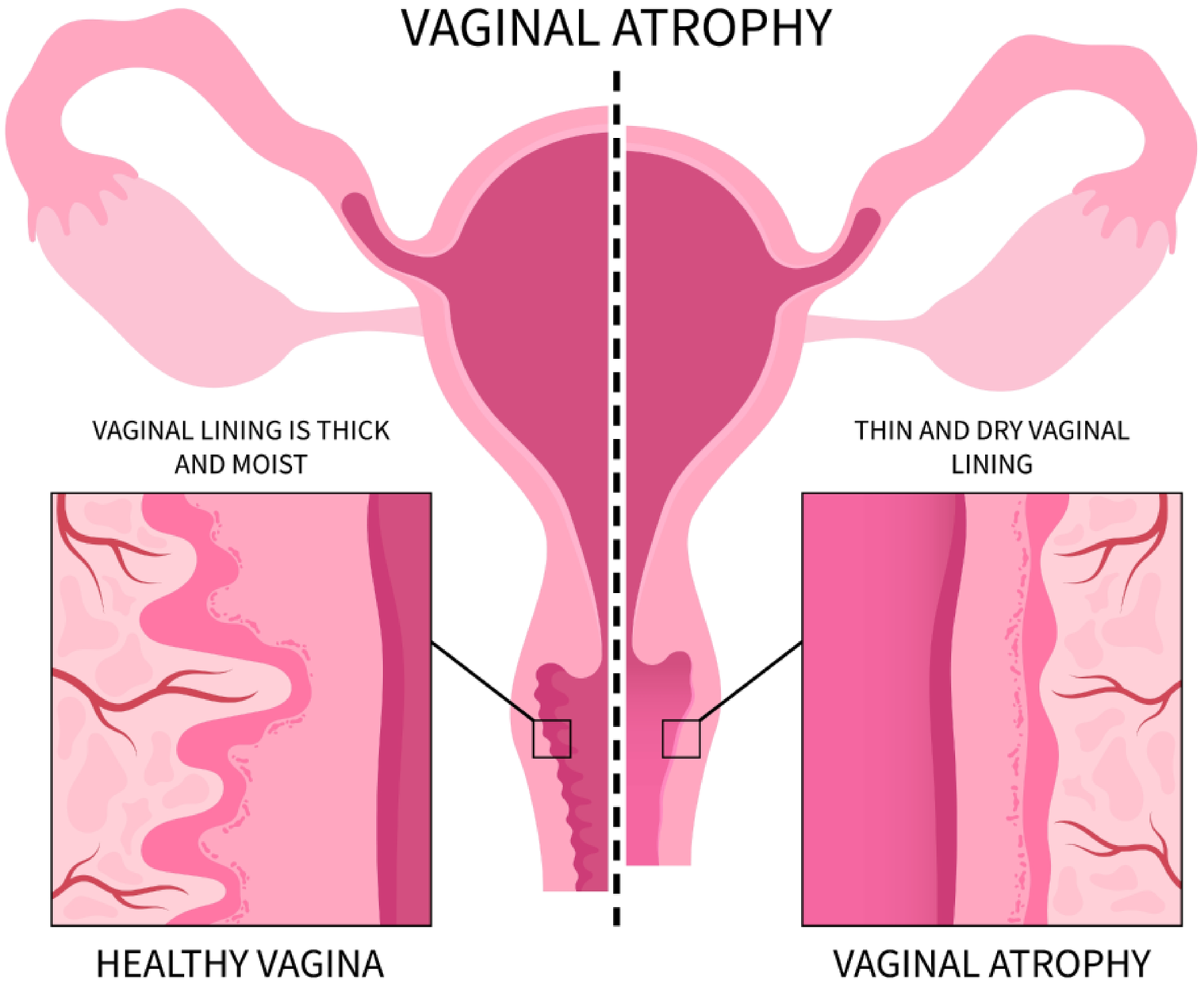
C/O Dr. Ksenija Martinec

Genitourinary Syndrome of Menopause (GSM)

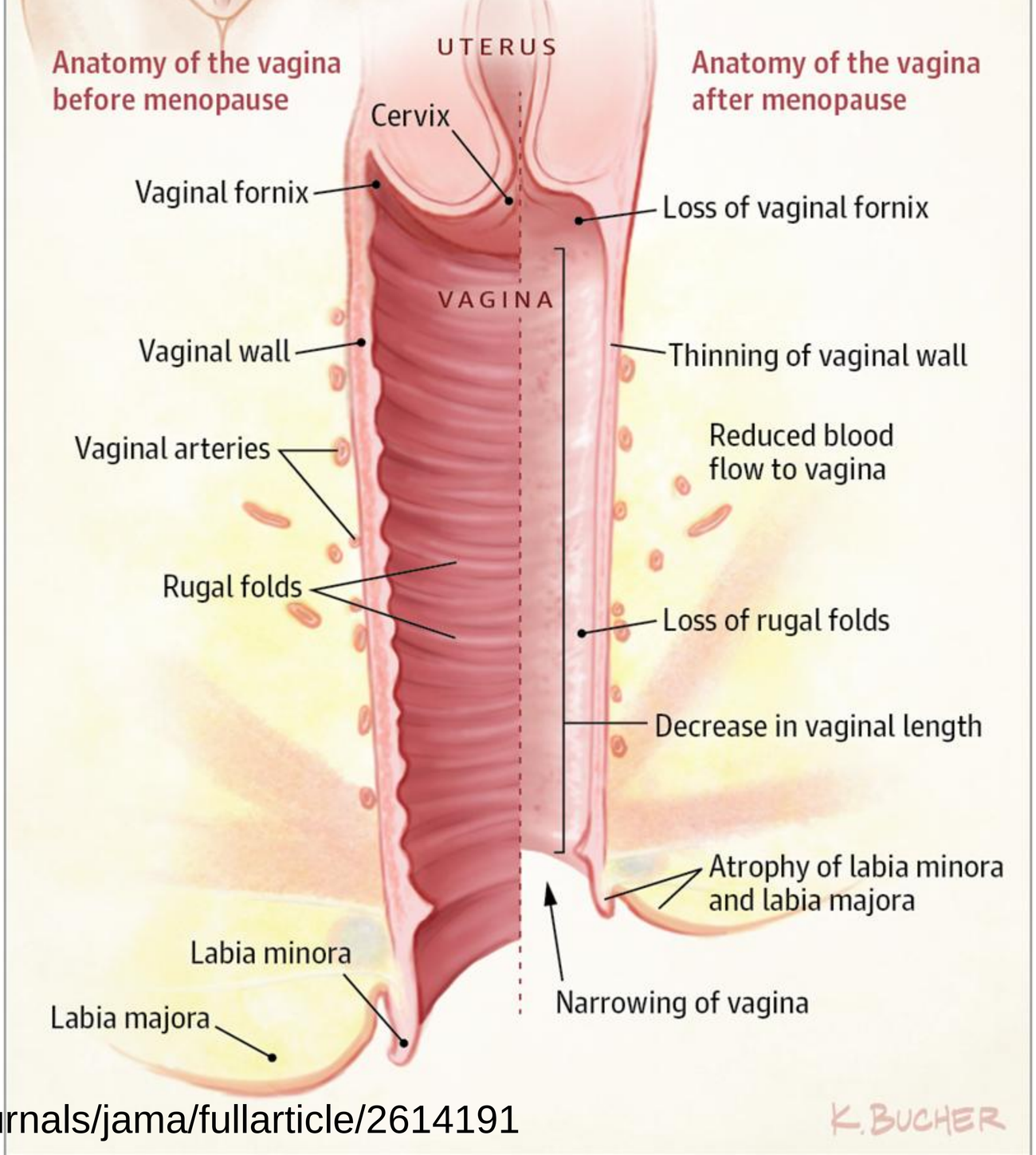
- GSM includes both vulvovaginal and lower urinary tract symptoms, due to decreased estrogen levels during menopause
- Symptoms and signs include: vaginal atrophy, dryness, burning, itching, irritation, dyspareunia, urinary frequency or urgency, and increased risk of urinary tract infection (UTI)
- Estimated to affect up to 77% of women*, but is often under-reported, under-diagnosed and under-treated
- A US survey in 2017** indicated 50% of women experiencing GSM had never used any therapy to address symptoms

*Crandall CJ et al. Management of menopausal symptoms: a review. JAMA 2023;329(5):405-20.

** Kingsberg SA et al. THe Women's EMPOWER survey: identifying women's perceptions on vulvar and vaginal atrophy and its treatment. J Sex Med 2017;14(3):413-23. Pub 2017 Feb 12



https://continentalhospitals.com/diseases/vaginal-atrophy/



https://jamanetwork.com/journals/jama/fullarticle/2614191

TABLE 1 Common signs and symptoms of GSM

Symptoms	Signs
Vaginal dryness	Loss of vaginal rugae
Irritation, burning, itching of vagina and vulva	Vaginal tissue paleness
Decreased lubrication during intercourse	Thin, dry, friable tissue of vagina and vulva
Dyspareunia	Cervix smaller, retracted
Postcoital bleeding	Decreased size of labia minora
Dysuria	Decreased pubic hair density
Increased urinary frequency and urgency	Prominent urethral meatus Recurrent urinary tract infections

https://www.contemporaryobgyn.net/view/common-signs-and-symptoms-gsm

GSM - More Than Just a Physical Issue

Psychosocial and Relational Impact

- Women frequently report:
  - Reduced confidence and body image
  - Avoidance of sexual activity
  - Emotional distress and frustration
- These changes can extend beyond the individual to affect:
  - Intimate relationships
  - Partner connection and communication
  - Overall relationship satisfaction
- Partners may experience:
  - Uncertainty or concern about causing discomfort
  - Reduced intimacy and connection
  - Changes in sexual dynamics

GSM and Desire Discrepancy

- Menopause-related sexual symptoms affect intimacy, confidence, and partner connection
- Sexual desire discrepancy is associated with lower relationship satisfaction
  - Mark KP. J Sex Marital Ther. 2015;41:214–229 The relative impact of individual sexual desire and desire discrepancy on satisfaction in heterosexual couples.
  - Kingsberg SA et al. J Womens Health. 2019;28:432–443. Journal of Women’s Health (Larchmt). 2019;28(4):432–443 Female sexual health: Barriers to optimal outcomes and a roadmap for improved patient–clinician communication.
  - Differences in sexual desire between partners are consistently associated with lower sexual satisfaction and relationship quality

Screening and Scoring

- The 2020 Menopause Society guideline recommends GSM education and screening for all perimenopausal and postmenopausal woman
- Studies use various scoring systems for GSM:
  - **Female sexual function index (FSFI)**
  - Vaginal health index
  - Vaginal maturation index
  - Urogenital distress inventory
  - Vulvovaginal symptom questionnaire
  - VAS/VuAS symptom scales
  - Day-to-Day impact of vaginal aging (DIVA)
  - Patient global impression of improvement
  - SF-36 (quality of life)

Female Sexual Function Index (FSFI)

- Measures sexual function across multiple domains:
  - Desire
  - Arousal
  - Lubrication
  - Orgasm
  - Satisfaction
  - Pain
- Total score range: 2.0 - 36.0
- Lower scores = worse sexual function (<26.5 suggests sexual dysfunction)

Treatment of GSM

Non-Hormonal Options

- Non-hormonal vaginal therapies are recommended first-line treatments for woman with less severe GSM
- Include:
  - Moisturizers
    - Regular use for maintenance: 2-3 times per week for at least 4 weeks
    - Not covered by most private or public drug plans
  - Lubricants
    - Used as needed for sexual activity

Treatment of GSM

Non-Pharmacologic Therapies

- Gentle vulvovaginal hygiene
  - Avoid perfumed products and soaps, toilet paper selection
  - Wash with water in squirt bottle
- Regular sexual touch (alone or with partner)
- Vaginal dilators
- Pelvic floor physiotherapy

Treatment of GSM

Vaginal Estrogen Therapies

- Low-dose vaginal estrogen therapies are recommended for women with moderate-to-severe GSM, recurrent UTIs, or for individuals with persistent symptoms despite non-hormonal treatments
- A number of trials note improvement in symptoms in the range of 60-80%
- Options include estrogen creams, tablets, rings, and gels
- Other than the ring, all versions are prescribed with an initial loading dose, followed by maintenance dosing, based on symptom control
- Initial benefits can be seen within the first few weeks, but full effects typically noted after 12-16 weeks of regular use
- Can be continued indefinitely at the lowest effective dose

Treatment of GSM

- Systemic hormone therapy for vasomotor symptoms may not address vulvovaginal concerns due to insufficient concentration of estrogen in urogenital tissues
- Can safely add low-dose vaginal estrogen therapy to systemic hormone therapy
- Recurrent UTIs:
  - Commonly defined as 3 or more UTIs in 1 year, or 2 or more UTIs in 6 months
  - Vaginal estrogen provide significant reduction in risk of recurrence vs placebo over 6-12 months in post menopausal women (meta-analysis)
  - Systemic estrogen did not provide the same improvements

Treatment of GSM

Systemic Absorption and Black-Box Warnings

- Systemic absorption of low-dose vaginal estrogen is minimal
- Initially atrophic tissue may lead to some systemic absorption, but decreases as vaginal tissues heal
- Do not require a progestogen for endometrial protection
- FDA removed the black-box warning on all menopause hormone therapies, including low-dose vaginal estrogen, for stroke, blood clots and breast cancer
- Health Canada has yet to update labeling to reflect this change

Newer Pharmacologic Therapies

Ospemifene

- Selective estrogen receptor modulator
- Oral tablet, once daily with food
- Agonistic effects on vaginal epithelium, bone and endometrium
- Antagonistic effects on other tissues such as breast
- Can cause vasomotor symptoms as a side effect
- Roughly $50 per month

Newer Pharmacologic Therapies

Prasterone

- Sex steroid precursor converted to estrogen and androgens
- Vaginal ovule, once daily
- Acts locally in vaginal endothelium as estrogen and androgen agonist
- $100-150 per month

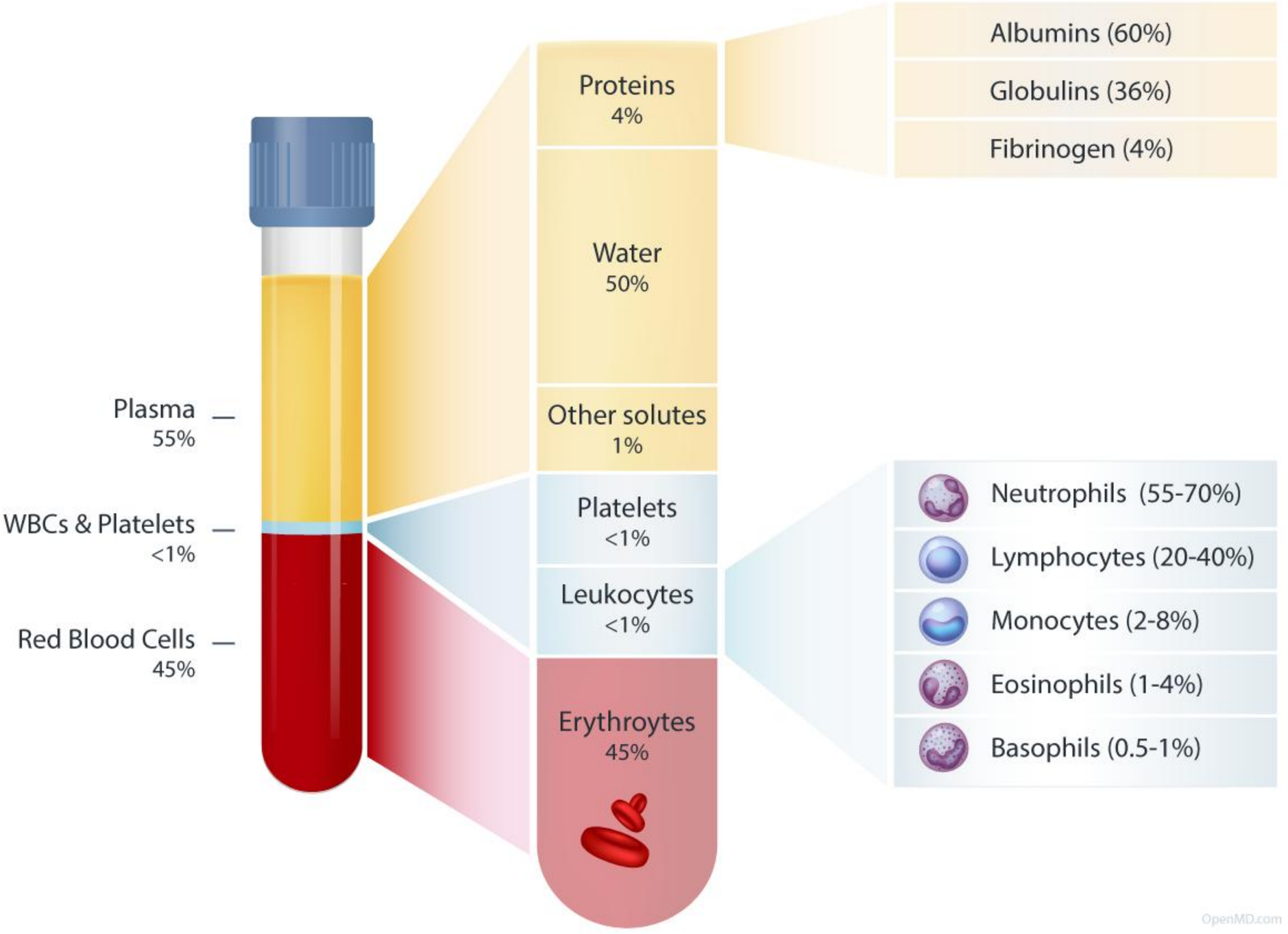
- No head-to-head trials comparing ospemifene to prasterone, they perform similarly in placebo-controlled trials
- Considered third-line treatment options after non-hormonal and low-dose estrogen treatments

GSM in Breast Cancer Survivors

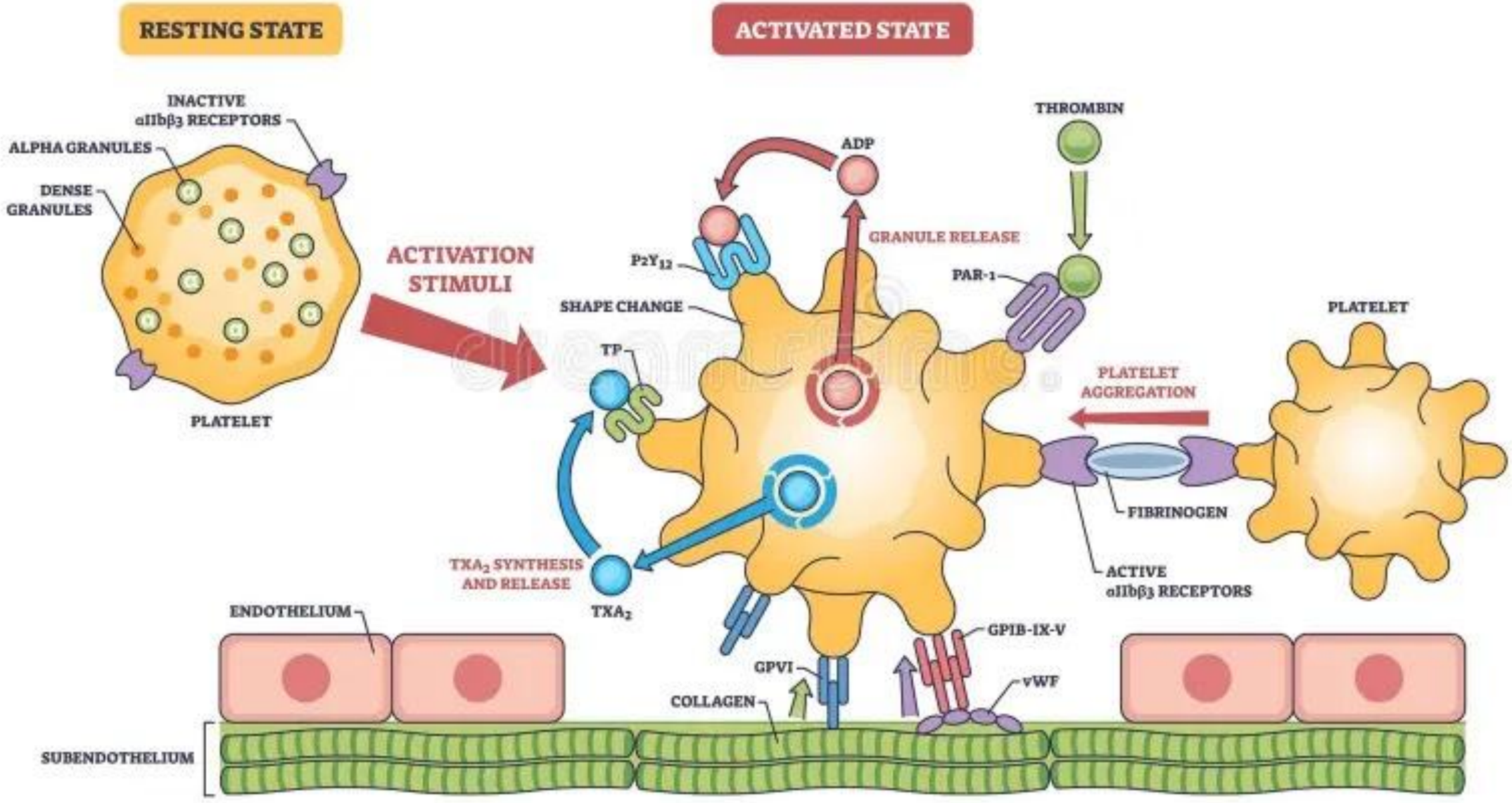
- Non-hormonal therapies are first-line
- Can consider low-dose vaginal estrogen (LDVE) on an individual basis, use is supported by the Society of Obstetricians and Gynaecologists of Canada
- Several recent large, population-level studies indicate LDVE does not affect life expectancy in woman with a history of breast cancer
- Those taking tamoxifen with LDVE do not have increased risk of breast cancer recurrence
- Those taking aromatase inhibitors (eg. Letozole, anastrozole) with LDVE were associated with higher risk breast cancer recurrence but did not appear to affect mortality

Platelet-Rich Plasma (PRP)

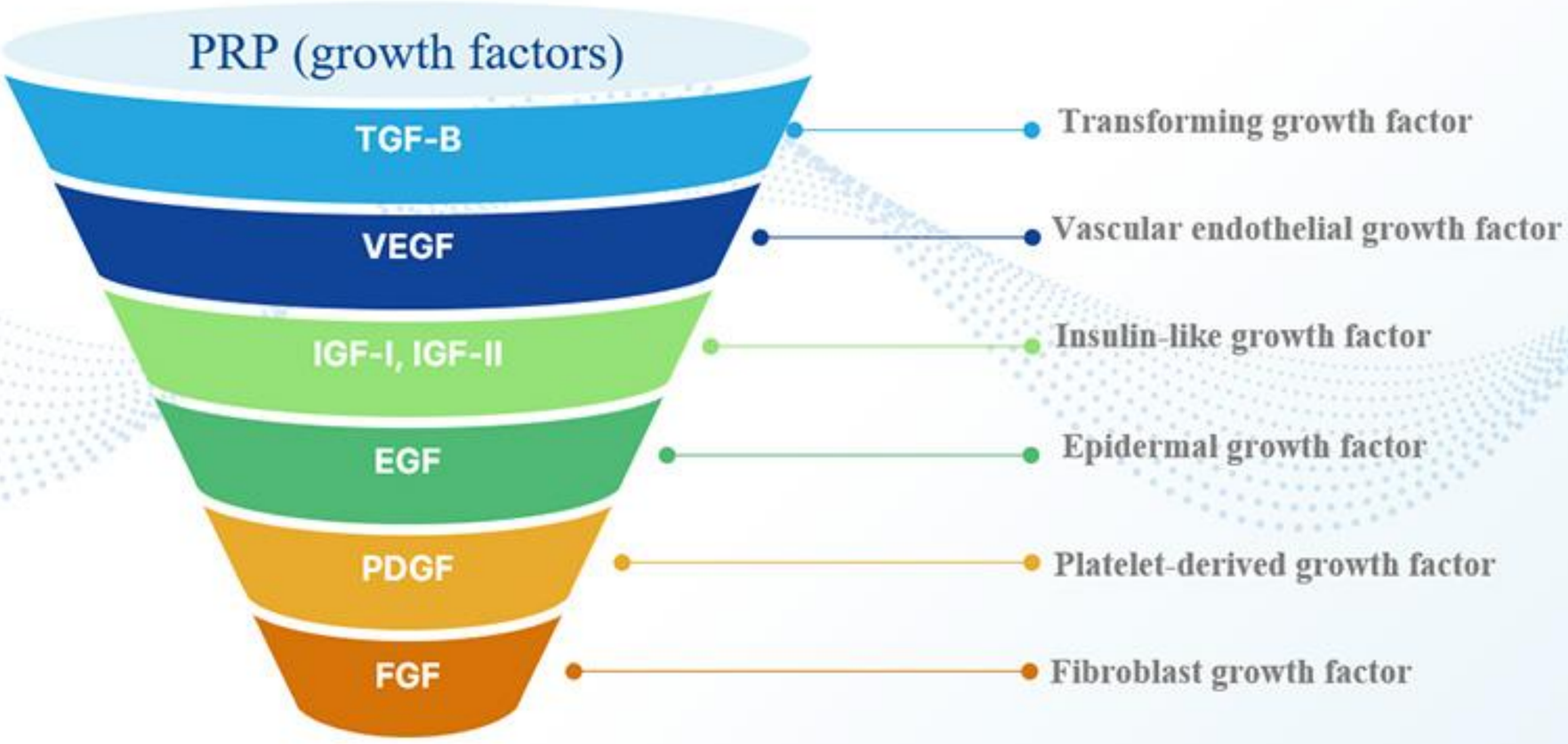
- First described as a blood product in 1954 by Kingsley et al
- Defined as plasma with platelets exceeding 1million/uL in every 5cc of plasma
  - Normal is 150,000 to 450,000/uL of blood
- Contains growth factors and cytokines
- Induces angiogenesis and facilities tissue repair due to supra-physiologic levels of growth factors released by activated platelets
- Promotes wound healing, stimulates angiogenesis, enhances collagen production, reduces inflammation


Plasma
55%
WBCs & Platelets
<1%
Red Blood Cells
45%
Proteins
4%
Water
50%
Other solutes
1%
Platelets
<1%
Leukocytes
<1%
Erythroytes
45%
Albumins (60%)
Globulins (36%)
Fibrinogen (4%)
Neutrophils (55-70%)
Lymphocytes (20-40%)
Monocytes (2-8%)
Eosinophils (1-4%)
Basophils (0.5-1%)

PLATELET ACTIVATION



Effects of PRP

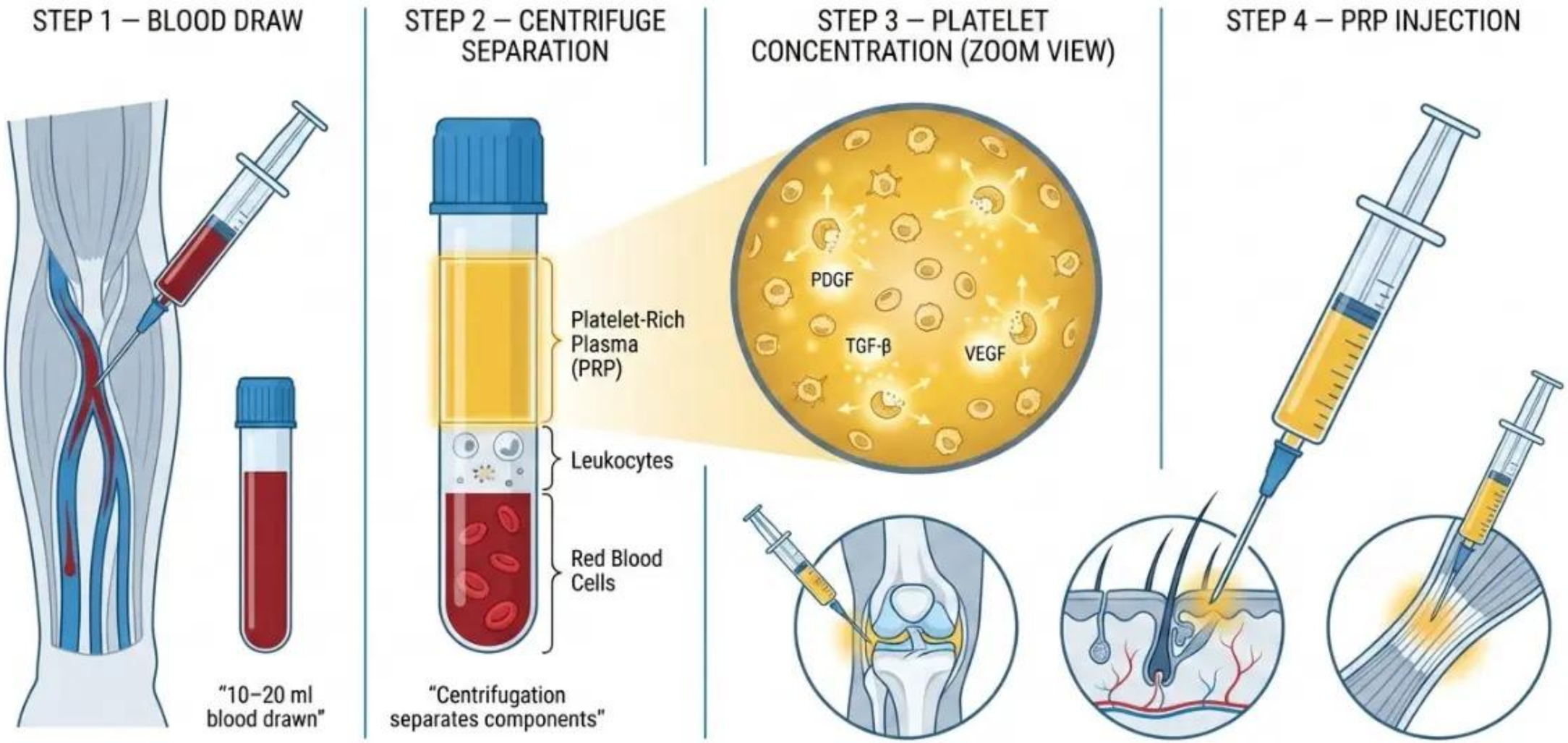


PRP and Growth Factors

Proposed Mechanisms of Repair

- TGF-β (Transforming Growth Factor-Beta): Promotes collagen synthesis and tissue remodeling, also plays a role in regulating inflammation and wound healing
- VEGF (Vascular Endothelial Growth Factor): Stimulates angiogenesis (new blood vessel formation), improving tissue perfusion and oxygenation
- IGF-I / IGF-II (Insulin-like Growth Factors): Support cell proliferation and tissue repair, and enhance collagen production
- EGF (Epidermal Growth Factor): Promotes epithelial cell growth and regeneration, helping improve mucosal integrity and surface healing
- PDGF (Platelet-Derived Growth Factor): Recruits fibroblasts and other repair cells to the treatment area and stimulates collagen and extracellular matrix production
- FGF (Fibroblast Growth Factor): Enhances fibroblast activity, angiogenesis, and tissue regeneration

PLATELET-RICH PLASMA (PRP) THERAPY PROCESS



https://mymedicineadvisor.com/health/prp-therapy-results/

PRP as Established Medical Therapy

- Clinical use developed in hematology in 1970s
- Introduced into surgery in 1980-1990s
- Now used across multiple specialties

PRP in Orthopaedics & Sports Medicine

- First major clinical case in 1990s
- Used in tendinopathy, knee osteoarthritis, muscle injuries
- Evidence:
  - >50 RCTs and >20 meta-analyses provide evidence of moderate quality, condition-specific
- Strongest support for lateral epicondylitis and mild-moderate knee OA
- Protocols were heterogeneous

PRP in Oral & Maxillofacial Surgery

- First used 1980-1990s, bone grafting, oral surgery
- Indications: bone regeneration, dental implants, sinus lift procedures, periodontal surgery
- Evidence: dozens of RCTs and multiple systemic reviews report moderate evidence supporting improved healing, often used as adjunct therapy
- Benefits were variable depending on procedure

PRP in Dermatology and Wound Healing

- First used 2000s onward
- Indications: chronic wounds, scar revision, skin rejuvenation
- Evidence: growing number of RCTs (>30 in wound healing alone!) and multiple meta-analyses
- Meta-analyses show improved healing rates in chronic wounds
- Protocols are heterogeneous

PRP in Hair Restoration (Androgenic Alopecia)

- First used 2000s
- Indications: androgenic alopecia, alopecia areata
- Evidence: >20 RCTs and multiple meta-analyses
- Noted improvement in:
  - Hair density
  - Hair thickness
- Requires repeat treatments

Fig. 1. A 46-year-old woman with androgenetic alopecia, before and 3 months after 3 platelet-rich plasma treatment sessions.

PRP in Other Medical Fields

- Other fields under exploration:
  - Urology/sexual medicine
  - Ophthalmology
  - Cardiac Surgery
  - Peripheral nerve regeneration

PRP in GSM (vulvovaginal atrophy)

Abdel Hamid et al, 2025 — PRP vs saline placebo for vulvovaginal atrophy

- Design: Prospective, double-blinded randomized controlled trial
- Population: 60 postmenopausal women with vulvovaginal atrophy, enrolled at Ain Shams University Hospital from August 2019 to May 2021
- Intervention: 30 received intramucosal PRP injections; 30 received saline placebo
- Follow-up: 4 months
- Primary outcome: FSFI; SF-36 quality-of-life domains were also assessed

PRP in GSM (vulvovaginal atrophy)

Abdel Hamid et al, 2025 — PRP vs saline placebo for vulvovaginal atrophy

- Results: Baseline FSFI was similarly low in both groups
  - At 4 months, FSFI improved significantly in the PRP arm
  - Domain-level improvements were seen in lubrication, satisfaction, and pain, but not in desire, arousal, or orgasm
  - Several SF-36 domains also improved in the PRP group
- Limitations: Single center, modest sample size, short follow-up, VVA-focused rather than full-spectrum GSM
- The authors conclude PRP is promising but requires larger RCTs before standard use

PRP in GSM (vulvovaginal atrophy)

Atlihan et al, 2025 — topical estrogen vs PRP for postmenopausal vaginal atrophy

- Design: Comparative clinical study; not randomized
- Population: 66 postmenopausal patients with VVA: 36 treated with topical estrogen, 30 treated with PRP. Importantly, the PRP group had previously received topical estrogen without adequate response
- Intervention: Topical estrogen vs PRP injections
- Follow-up: Assessments at 4-week intervals through 12 weeks
- Outcomes: VHI, FSFI, VSQ, and VAS

PRP in GSM (vulvovaginal atrophy)

Atlihan et al, 2025 — topical estrogen vs PRP for postmenopausal vaginal atrophy

- Results: At 12 weeks, FSFI and VSQ results in the PRP-treated group differed significantly from the topical estrogen group
- The authors conclude PRP is a safe and effective minimally invasive monotherapy and may be relevant for women with contraindications to hormone therapy or inadequate response to estrogen
- Limitations: Because the PRP group was composed of prior estrogen non-responders rather than randomized peers, this is **not** a head-to-head efficacy trial in the strict sense

PRP in GSM

Waghe et al, 2024 — review of PRP in GSM

- Design: Review of the existing literature
- Search scope: PubMed, Scopus, and Google Scholar up to April 2023
- Studies included: Limited number of clinical studies (primarily small prospective and pilot studies).
    - No large randomized controlled trials identified

PRP in GSM

Waghe et al, 2024 — review of PRP in GSM

- Key findings:
  - Consistent trend toward improvement in: Vaginal dryness and discomfort, Sexual function, Patient-reported outcomes
  - Strong biologic plausibility based on: Growth factor release, Tissue regeneration mechanisms
- Limitations: Small sample sizes, Lack of randomized controlled trials, Heterogeneity in PRP preparation and protocols, Short follow-up durations
- **Main message: PRP is biologically plausible and may be considered in women with contraindications to hormonal therapy, but the evidence base remains limited and future randomized trials are needed**

PRP in Breast Cancer Survivors

Chen et al, 2025 — PRP for GSM in breast cancer survivors

- Design: Prospective, single-arm pilot study
- Population: 20 breast cancer survivors (stage 0–III) with vaginal dryness with or without dyspareunia; mean age 53.6 years. Eighty-five percent had hormone receptor–positive disease, and 65% of those were taking an aromatase inhibitor.
- Intervention: One-time treatment with 7 mL autologous PRP injected throughout the vaginal canal and posterior fourchette into 35 sites
- Follow-up: 6 months
- Primary outcome: Safety and feasibility. Secondary outcomes included VMI, VHI, VAS/VuAS, DIVA, FSFI, UDI-6, vaginal caliber, and PGI-I

PRP in Breast Cancer Survivors

Chen et al, 2025 — PRP for GSM in breast cancer survivors

- Results:
  - No serious adverse events occurred; transient spotting, irritation, discharge, burning, cramping, and mild pain resolved within 24 hours.
  - At 6 months, VAS/VuAS, FSFI, UDI-6, DIVA, VHI, and total scores improved significantly; VMI did not significantly change. Ninety percent increased vaginal caliber, and 95% reported symptomatic improvement on PGI-I
- Limitations: Uncontrolled pilot design, small sample, survivorship population limits generalizability

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Symptoms of Genitourinary Syndrome of Menopause (GSM)

Vaginal Symptoms

- Dryness
- Burning
- Itching inside and around the vagina
- Irritation
- Pain and pressure

Urinary Symptoms

- Leaking urine
- Pain or burning when you pee
- Needing to pee more often than usual
- Urinary tract infections

Sexual Symptoms

- Loss of sex drive
- Painful sex
- Spotting or bleeding during or after sex
- Inability to reach orgasm

https://www.everydayhealth.com/womens-health/genitourinary-syndrome-of-menopause/

PRP in GSM

- Autologous concentrate of platelets/growth factors
- Proposed effects on angiogenesis, fibroblast signaling, collagen remodeling, tissue healing
- Theoretical relevance to atrophic, hypoestrogenic tissue
- Key caveat: biologic plausibility is not the same as proven clinical efficacy, although success in other medical applications is encouraging
- **Bottom line:** evidence is **promising but preliminary**. Most data are small, heterogeneous, and short-term. There are encouraging early studies, including one breast-cancer survivor pilot, and ongoing randomized trials, but PRP for GSM is **not yet supported by robust, mature RCT evidence**

PRP in GSM

Where does it fit into standard therapies?

- First-line:
  • Vaginal moisturizers and lubricants
- Second-line:
  • Vaginal estrogen
- Third-line:
  • Vaginal ospemifene
  • Prasterone
- Adjunctive / supportive care:
  • Pelvic floor physiotherapy
  • Sexual health counselling
  • Lifestyle and behavioral interventions
- PRP is **not first-line therapy**, but may be considered in selected patients:
  - Patients who **cannot use estrogen** (e.g., breast cancer survivors, contraindications, inability to apply)
  - Patients who are not interested in hormonal therapy
  - Patients with persistent symptoms despite standard treatment

PRP for GSM

Available locally at Medical Aesthetics of Muskoka - Dr. Kents

- Potential advantages:
  - Non-hormonal
  - Minimally-invasive (topical freezing, injected locally)
  - Uses autologous tissue
- Patients undergo 1-3 treatments, spaced 1-3 months apart
- Maintenance every 12-18 months, as needed
- $1300 per treatment
  - discount of 15% provided if repeat treatment performed in recommended time frame

GSM

Still discovering, still evolving

- Genitourinary Syndrome of Menopause (GSM) is common and under-recognized, with meaningful impact on quality of life
- GSM affects more than physical symptoms — it can influence confidence, intimacy, relationships, and overall well-being
- Despite advances in medicine, aspects of women’s health remain incompletely understood and underrepresented
- Platelet-Rich Plasma (PRP) is well-established in other areas of medicine, with a growing body of evidence in fields such as orthopedics, wound healing, and dermatology
- In GSM, PRP shows biologic plausibility and consistent early signals of benefit, but current evidence remains limited and evolving
- At present, PRP is best considered an adjunctive or alternative option for certain patients