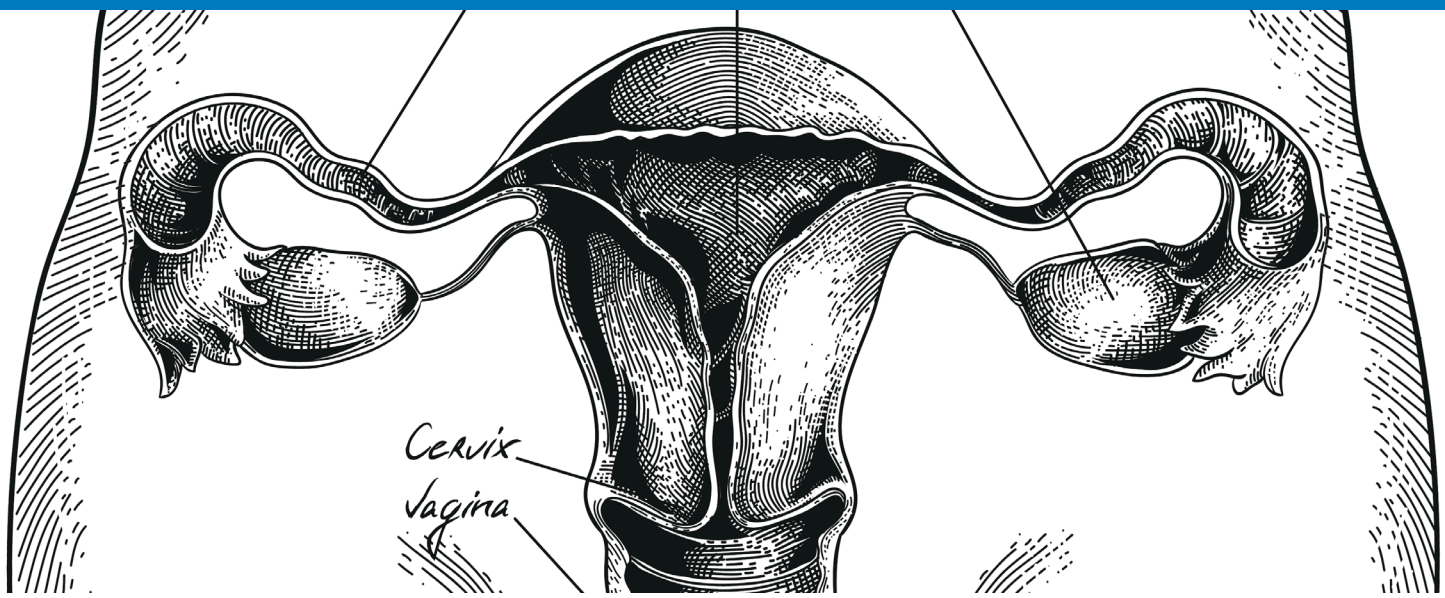
Vaginal Atrophy and Sexual Function



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This article discusses management options for vaginal atrophy and the importance of considering these in women for optimal sexual function.

Introduction

Vulvovaginal dryness is a common problem after the menopause. It can lead to painful sexual intercourse, vulval irritation and may contribute to bladder problems, such as recurrent urinary tract infections. Studies have shown that many Australian women do not recognise it as a treatable medical condition.[1] One recent Australian survey showed that only 5% of women aged sixty to sixty-five years were using the most effective treatment, that is topical oestrogen.[1] The International Menopause Society recently reviewed its guidelines for managing menopause.[2,3] Regarding vaginal atrophy, the Guidelines state: 'There are considerable data to support their (topical oestrogens) use in urogenital atrophy.'[2]

This short review will examine the normal physiology of the vagina and the impact of menopause on genitourinary atrophy. Effective therapies for this distressing problem will also be discussed.

Normal Physiology of the Vagina

The vagina is a fibromuscular tube lined by epithelium. It joins the cervix and uterus posteriorly to the vulva at front.[4,5] The

Take Home Messages

- There are considerable data to support the use of topical oestrogens in urogenital atrophy.
- Topical oestrogens should not be deposited deep in the vagina, but rather in the anterior portion, in order to minimise uterine exposure and to maximise the effect on the vulva, urethra and clitoral areas.
- Oestrogen creams may be best used by abandoning the applicator all together and placed on a finger instead. This is then inserted inside the anterior vagina; some cream should also be smeared onto the vulval skin.
- Patients who have had breast cancer should use non-hormonal moisturisers first and topical oestrogen as a last-resort.
- Vulval dryness may respond to soap-free washes, using plain moisturisers on the vulva and intravaginal moisturiser products. Natural oils (such as coconut oil or olive oil) can be effective lubricants.

anterior portion of the vagina has markedly different properties to the posterior vagina, reflecting their differing embryological origins. The anterior vagina arises from the urogenital sinus and the posterior vagina from the Mullerian ducts.[5] Interestingly, the anterior vagina, clitoris and urethra all share a common blood supply and innervation (the anterior branch of the pudendal nerve). The vulva, vagina and clitoris are all covered in squamous epithelium. During sexual arousal, engorgement of all these regions occurs.[5] There is a complex network of blood vessel surrounding the vagina, especially anteriorly. As shown in the Figure 1, the clitoral vascular unit surrounds the vulva on both sides.

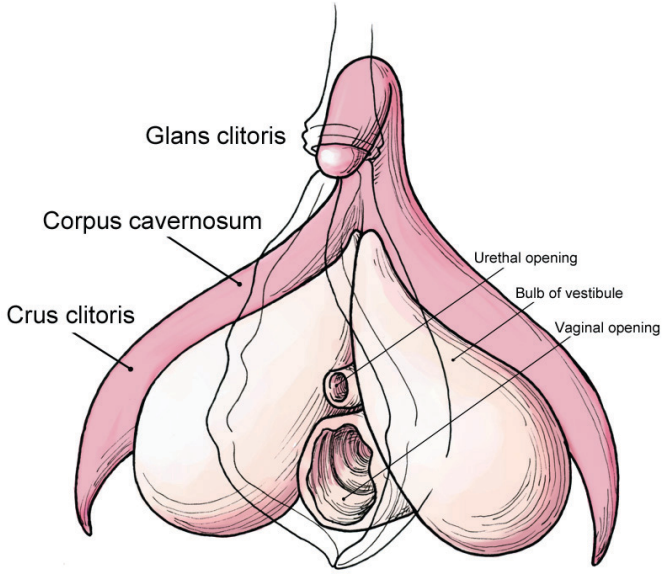

Figure 1. Anatomy of the vulva and clitoris
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During sexual arousal, the vaginal and urethra both release secretions[5] that make penetrative intercourse much more comfortable for the woman. It has been shown that water transfer across the vaginal mucosa is controlled by specific conduits called 'aquaporin water channels'.[6] The pelvic floor muscles support the vagina, bladder and rectum and also play an important role in sexual function.[4,5] All these structures (the clitoris, the pelvic floor muscles and the vaginal epithelium) have sex-hormone receptors (mostly oestrogen receptors; some parts of the pelvic floor muscles have androgen receptors).[7-10]

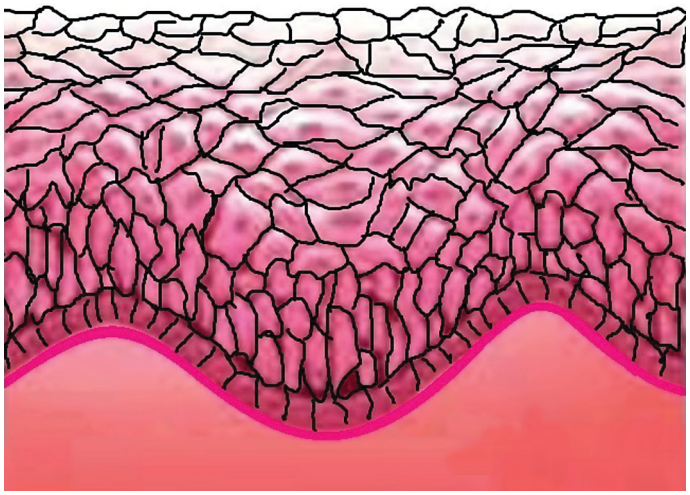

Figure 2. Diagram of vaginal epithelium of a reproductive aged woman. Note the thick superficial epithelial layer.
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During the reproductive years, the vaginal epithelium is thick and moist, in response to stimulation by oestrogen (see Figure 2).

After menopause, the vaginal epithelium markedly thins[11] (see Figure 3), as does the supporting vaginal tissue. This atrophic epithelium often cannot support sexual intercourse and this then becomes dry and painful. Topical oestrogens are very effective at reversing the problem.[11]

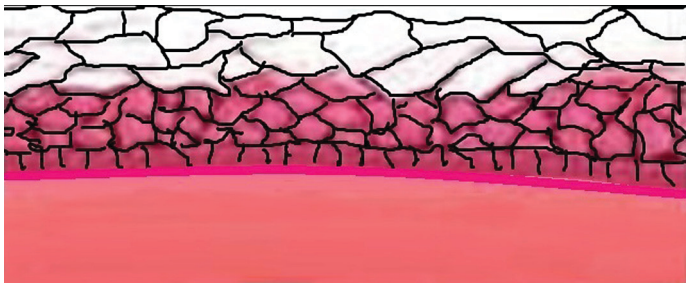

Figure 3. Diagram of vaginal epithelium of an untreated, postmenopausal woman. Note the thinning of the superficial epithelial layer.
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Finally, the healthy vagina has a symbiotic relationship with several bacteria, most notably, lactobacillus[12-14] and typically, one or two species dominate. These bacteria produce lactic acid that helps to maintain an acidic environment within the vagina. This aids the reduction of pathological microorganisms. Interestingly, there are data to suggest that cross-species chemically communicate with each other.[14] It seems likely that the healthy vaginal epithelium releases chemical signals, 'attracting' the right species of lactobacillus.

Table. The Vagina as a Delivery System.[16]

- The vagina is a primary target for sex hormones and so topical hormone therapies can affect the vagina directly.
- Some vaginal delivery systems have systemic effects (e.g. NuvaRing®) because of exposed surface area and positioning.
- The vagina has a large surface area (around 95cm^2) and has an extensive surrounding venous plexus that is in close proximity to the vaginal arterial supply. In the upper vagina, veins merge into the uterovaginal plexus that eventually drains into the iliac vessels. The anterior vaginal veins merge into the haemorrhoidal and pudendal internal plexus. This difference partially explains the difference in medication distribution, depending upon where in the vagina the medication is placed.
- Absorption across the vagina is governed by factors such as the molecular weight of the medication, liposolubility, duration and surface area of exposure.
- The concentration gradient between medication and blood is a primary determinant of absorption through the vaginal wall. Thus, for example, the absorption of two caps of progesterone 100mg via the vaginal epithelium is not exactly the same as one cap of progesterone 200mg.
- Physiological factors, such as the phase of the menstrual cycle and the vaginal pH will alter absorption.
- Compared to the intestinal epithelium, the vagina has low metabolic activity. Compared to oral administration, vaginal delivery of progesterone, for example, results in higher serum levels and a more potent uterine effect, while levels of 5α and 5β metabolites are lower. This leads to fewer side-effects (such as sedation and moodiness) with vaginal administration of progesterone compared to oral administration.
- Steroids absorbed through the vagina may have two different pathways:

  a. Systemic:

  Rapid absorption (e.g. progesterone in oil administered via the vagina results in peak serum levels one to two hours after administration, followed by more sustained levels when compared to oral administration). Avoidance of hepatic first-pass metabolism results in a greater bioavailability of the medication with little metabolism, hence there is minimal impact on liver proteins such as clotting factors.[16]

  b. Regional distribution:

  i. Uterine-first-pass effect: drugs delivered to the upper third of the vagina tend to pass directly to the uterus. This is largely due to a sharing of upper vaginal vessels and uterine vessels.[16] For example, the plasma levels of vaginally administered progesterone are higher in the uterine arteries than in the radial arteries.[16]

  ii. Preferential distribution to the pelvis: Vaginal danazol is an effective treatment for endometriosis because the drug is preferentially distributed to the uterine, broad ligament, ovarian and utero-ovarian pedicles.

  iii. Topical medications placed in the lower third of the vagina are delivered to the periurethral, vulval and clitoral areas.

Lactobacilli also produce hydrogen peroxide, hydroxyl radicals and probiotics, all of which help to control the vaginal microbiome.[12-14] After menopause, the lactobacilli usually disappear and the vagina tends to be colonised by bowel flora (such as E. coli). [12-14]

In summary, much of the female sexual response is regulated by oestrogens, although androgens also have an important role. The untreated postmenopausal state typically results in vulvovaginal thinning and loss of lubrication, resulting in painful intercourse.

The Vagina as a Delivery System

Cicinelli and colleagues have performed a number of studies examining the concept of the vagina as a delivery system.[15-17] Some of the pharmacokinetics of the vaginal route of delivery are summarised in the Table.[16]

In an elegant study, Cicinelli studied six women undergoing abdominal hysterectomy.[17] Three had their cervices sealed with surgical glue (to prevent transcervical transmission of medication). Each of the six had 0.2cc ^{99m}Tc-pertechnetate deposited in the upper third of the vagina and they were then placed in a nuclear medicine scanner. Evidence of radioisotope uptake in the uterus appeared after sixty minutes and peaked at approximately one hundred and twenty minutes to two hundred and ten minutes. The authors concluded that preferential vagina-to-uterus distribution is largely mediated by a counter-current vascular transfer mechanism, and not via the cervix.

The authors also studied Vagifem® (25mcg oestradiol vaginal tablets) and its positioning in different sites (either the upper or the lower third of the vagina).[15] They then investigated the impact on the uterine blood vessels (using Doppler) and also documented the systemic levels of oestradiol.[15] Oestradiol tablets placed in either vaginal position resulted in small, but significant rises in serum oestradiol levels. Placement of oestradiol in the upper vagina resulted in a significant decrease in pulsatility and resistance index of the uterine arteries, consistent with an oestrogenic effect. No such effect was seen with placement in the anterior vagina. They concluded that topical oestrogens should not be deposited deep in

References: 1. Ovestin Cream Approved Product Information 6 July 2016 **2.** Ovestin Pessaary Approved Product Information 6 July 2016 **3.** Ovestin Tablets Approved Product Information 6 July 2016 **4.** Suckling et al. 2006, Local oestrogen for vaginal atrophy in postmenopausal women (review). Cochrane Collaboration **5.** Sturdee DW, Panay N. Recommendations for the management of postmenopausal vaginal atrophy – on behalf of the International Menopause Society Writing Group.Climacteric 2010;Early Online, 1-14

the vagina, but rather in the anterior portion, in order to minimise uterine exposure and to maximise the effect on the vulva, urethra and clitoral areas.

Vaginal Hormone Therapies

Rahn has performed a meta-analysis of vaginal oestrogens for genitourinary symptoms after menopause.[18] He concluded that they are all effective and seem safe. He found some studies comparing vaginal moisturisers and topical oestrogens; the oestrogen products were significantly more effective.

As previously discussed, it seems prudent to instruct patients to place topical oestrogens in the anterior portion of the vagina. Creams such as Ovestin® may be best used by abandoning the applicator all together and suggesting that the patient place about a square centimetre of cream on a finger. They should then place that finger inside the vagina and smear the rest of the product onto the vulval skin. The Vagifem® introducer should probably not be placed deep inside the vagina, but rather, only about three to five centimetres inside. Both products are probably best used at night to avoid external spillage.

There is some controversy about the use of topical oestrogens after a diagnosis of breast cancer.[19] The American College of Obstetricians and Gynecologists suggests that such patients use non-hormonal moisturisers first and that topical oestrogen be used as a last-resort.[19] Topical dehydroepiandrosterone (DHEA) or laser therapy may be a better option for these patients.

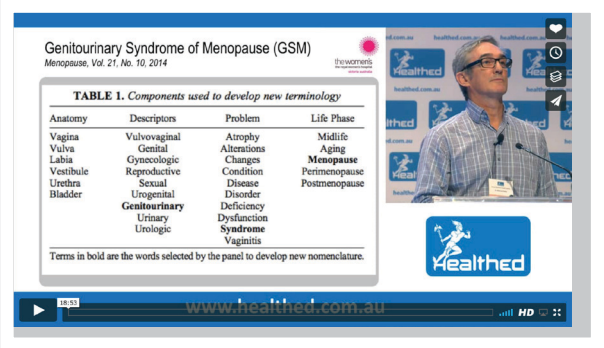
Pharmaceutical grade topical DHEA is not yet available in Australia.

Topical DHEA (6.5mg daily delivered as a pessary) has been shown to convert to oestrogen. This then acts on the vagina without any systemic effect on serum oestrogen or androgen levels. Measurements were performed by very sensitive technology (mass-spectrometry).[20,21] Pharmaceutical grade topical DHEA is not yet available in Australia. Laser therapy is discussed below.

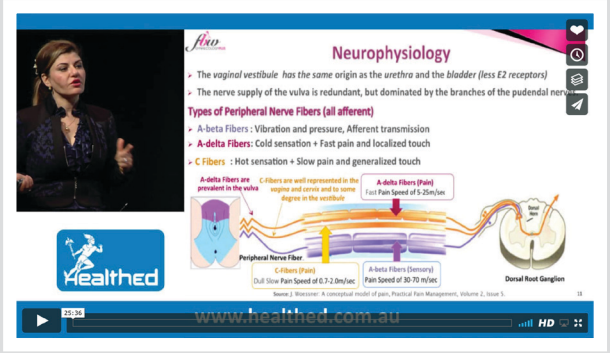
Non-hormonal Therapies for Vaginal Atrophy

Many Australian women wash with soap and this has marked drying properties. Some obtain relief from vulval dryness by simply bathing with soap-free washes, using plain moisturisers on the vulva and sometimes intravaginal moisturiser products (such as Replens®). Natural oils (such as coconut oil or olive oil) can be effective lubricants. Some women who have put up with marked

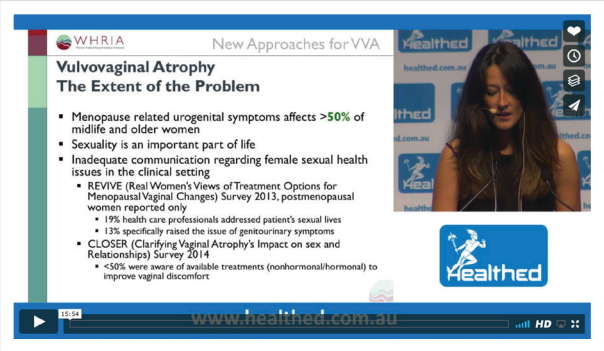
Video Resources



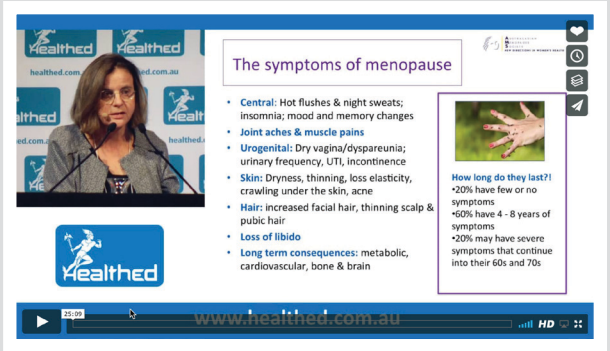
New Approaches for Management of Vulvovaginal Atrophy by Dr Marcus Carey



New Developments in the Management of Vaginal Atrophy & Dyspareunia by Dr Fariba Willison



Vulvovaginal atropy by Dr Yasmin Tan



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vaginal dryness for years develop pelvic floor myalgia (spasm). This can be usually managed by referral to a pelvic floor physiotherapist who can teach the patient how to relax their pelvic floor.

Natural oils (such as coconut oil or olive oil) can be effective lubricants.

Laser therapy may be useful for some women, for example, those who have had breast cancer.[22] Salvatore and colleagues used the microablative fractional CO_2 laser in an uncontrolled study of seventy-seven postmenopausal women who had symptoms of vulvovaginal atrophy.[23] Twenty of these women had ceased sexual activity because of discomfort. The subjects had three treatments, each four weeks apart. A 'treatment' involved firing 'laser dots' over different areas of the vagina and vulva. This was very well tolerated without anaesthesia. At the twelve-week follow-up, seventeen out of twenty women who had ceased sexual activity because of pain were able to resume intercourse. Sexual function scores significantly improved over the study period.

Athanasiou and colleagues recently published a study examining the effect microablative fractional CO_2 laser on vaginal flora[24]. At the end of a course of treatment, the vaginal pH fell and the prevalence of lactobacilli species increased. This novel therapy appears very promising, but further research is needed. Ideally a large, long-term (over years) randomised controlled trial is needed to confirm these results and to discover how long the therapeutic effect lasts.

Conclusions

Vulvovaginal atrophy after menopause is a major cause of distress for many post-menopausal women and their partners. Simple measures such as avoidance of soap and the use of moisturisers can help some. However, many need topical oestrogens such as Ovestin® or Vagifem® and oestriol pessaries. Ovestin® cream is best used by avoiding the applicator altogether and introducing a small amount of cream into the vagina with a finger and then smearing the residual cream onto the vulva. Vagifem® should ideally be introduced into the anterior portion of the vagina, and not deep into the fornices. For a small number of patients, the microablative fractional CO_2 laser may be helpful, although long-term studies are lacking.

Further Reading

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Declaration

Dr John Eden was commissioned by Healthed for this article. The ideas, opinions and information presented are solely those of the author. Dr John Eden declares no significant competing financial, professional or personal interests that might influence this article.

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