



OCULAR SURFACE DRYNESS IN WOMEN



An examination of the changing ocular surface through the stages of life.

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Strong epidemiologic evidence indicates that the female sex has a higher predilection for ocular surface dryness.¹⁻⁶ Risk factors for ocular surface dryness change and compound over a lifetime. Even changes in hormones can trigger flare-ups. But a firm understanding of key milestones in ocular surface dryness over the course of a woman's lifetime can guide eye care providers in recognizing when their female patients may need ocular surface support.

Author's note: This article focuses on the concept of biological sex and not gender. Sex is a classification given to biological organisms based on their chromosomal makeup and reproductive organs.^{1,7} Gender refers rather to an individual's self-representation as male, female, or other, reflected as societal and cultural characteristics given to behavior.^{1,7} For the purposes of this article, the terms female, male, woman, and man will reference sex characteristics, which play a crucial role in ocular surface dryness.

MILESTONE NO. 1: MATURITY

The ocular surface was made to be partially regulated by hormones. The cornea, conjunctiva, and tear glands all have receptors specific to testosterone, estrogen, and progesterone.⁸⁻¹⁸ The sex hormones that act locally are not all primarily sourced from the ovaries and testes but are also synthesized in the ocular tissues.⁸⁻¹⁷ This intracrine system modifies the adrenal sex steroid precursor dehydroepiandrosterone (DHEA) to generate estrogen and testosterone.⁸⁻¹⁷ The adrenal gland also supplies progesterone.^{8-11,17}

The difference in incidence of ocular surface dryness between men and women is largely attributed to the differences in levels and processing of hormones between the sexes. *Testosterone*, a member of the androgen family, is secreted in higher levels in men. Testosterone has positive effects on the ocular surface, mediating actions through alterations in gene activity.⁸⁻¹⁶ Conversely, estrogens are produced in much higher levels in premenopausal women, and the effects of estrogens on the ocular surface are varied.^{8-12,17} Estrogens have the largest effect on ocular surface dryness by interrupting the binding of the supportive testosterone. These two hormones have reverse actions. To a lesser extent, estrogens and progesterone have direct effects on the

TABLE 1. Sex Hormone Effects on the Ocular Surface of Men and Premenopausal Women

HORMONE	EFFECTS ON OCULAR SURFACE
Testosterone	<ul style="list-style-type: none">• Increases quantity of tear secretions (lacrima, meibomian, goblet cell)^{8-10,12-16}• Improves quality of tear secretions (lacrima, meibomian, goblet cell)^{8-10,12-16}• Suppresses inflammation of both the lacrima and meibomian glands^{8-10,12-16}• Downregulates hyperkeratinization of epithelial cells⁸⁻¹⁰
Estrogen	<ul style="list-style-type: none">• Helps corneal epithelial cells to reach maturation⁸⁻¹⁰• Stimulates goblet cell secretions^{8-10,12-16}• Interrupts binding of androgens^{8-10,12-16}• Decreases corneal sensitivity⁸⁻¹⁰• Decreases levels of meibomian and lacrima gland secretions^{8-10,12-16}
Progesterone	<ul style="list-style-type: none">• Decreases meibomian gland secretions^{1,8,9,17}• Unknown/conflicting reports in the literature on effect on the lacrima glands and goblet cells^{1,8-12,17}

ocular surface.^{8-12,17} The effects of sex hormones on the ocular surface can be seen in Table 1.

MILESTONE NO. 2: PREGNANCY

Pregnancy can elevate the risk for ocular surface dryness. Increases in estrogen, progesterone, and prolactin released from the placental tissues, ovaries, and pituitary gland are associated with temporary ocular surface dryness.¹⁸⁻²⁶ Ocular surface changes (Table 2) can occur throughout the 40-week pregnancy time span, but they most commonly arise in the third trimester, when hormone levels are highest.¹⁸⁻²⁷ Animal models have demonstrated that higher levels of estrogen, progesterone, and prolactin are associated with an increase in tissue-remodeling and proinflammatory cytokine circulation.^{23,24}

Ocular surface dryness can also be exacerbated in those with morning sickness. Both vomiting and the use of antinausea medications have ocular surface drying effects due to dehydration.¹⁸

Most ocular surface changes will go away within 3 months of giving birth, as pregnancy hormones dissipate and mild corneal deviations resolve.^{18,21-23,26}

It is important to educate patients that any alterations made to glasses or contact lens prescriptions during pregnancy are unlikely to be permanent. If a patient’s refractive changes (usually a mild myopic shift)²⁰ are deemed unsafe for driving, providing a small supply of daily contact lenses may help. Should contact lens intolerance occur, a temporary change in the patient’s spectacle lenses may be preferable. Referrals for refractive surgery should be postponed, along with prognoses for cornea ectasia, keratoconus, and nonurgent glaucoma, until the cornea stabilizes postpartum.^{18,19}

Treatments for ocular surface dryness must be balanced with doing no harm to the growing baby. Palliative and mechanical choices are often favored by both patient and practitioner during pregnancy.^{18,19,28} Nonpreserved artificial tears can offer safe temporary relief. Meibomian gland expression (with vectored thermal pulsation or handheld LED) is not directly contraindicated but has not been studied in pregnant women.

In the event that topical pharmaceuticals such as topical steroids, cyclosporines, and antiallergy

drops are needed to help combat corneal edema and/or irritation, punctal occlusion should be performed to limit systemic absorption.¹⁹ None of the aforementioned topical drops exceed the FDA’s pregnancy category C, wherein “the potential benefits may justify the use of the drug in pregnant women despite the potential risks.”¹⁹

MILESTONE NO. 3: MENOPAUSE

Menopause is a necessary female milestone that is the result of the natural aging of the ovaries. It is a 2-to-8-year process that marks the end of reproductive ability and is signified by cessation of the menstrual cycle for 12 or more months.^{29,30} Women usually reach menopause between the ages of 40 and 55 years.^{29,30} The ovaries stop secretion of estrogen and testosterone. Small amounts of these hormones are still produced locally within peripheral tissues by modifying DHEA from the adrenal glands.¹²

By the onset of menopause, age-related decreases in DHEA and progesterone have already occurred, with a loss of 60% from peak secretion.¹² This combined loss of DHEA from the pituitary gland and hormones from

TABLE 2. Potential Ocular Surface Changes in Pregnancy

Cornea	<ul style="list-style-type: none"> • Increased thickness^{18,21,26} • Increased volume^{18,21} • Increased curvature, mainly steepening^{18,21,25} • Reduced sensitivity^{18,21,22}
Lacrimal Glands	<ul style="list-style-type: none"> • Reduction in secretions^{18,24} • Acinar tissue destruction^{18,24}
Meibomian Glands	<ul style="list-style-type: none"> • Reduction in secretions^{18,19}

the ovaries has been correlated with worsening of ocular surface dryness signs and symptoms.¹ A loss of androgens that results in tear deficiency seems to be a sex-linked condition, as androgen deficiency in men does not reduce tear secretion.^{1,12}

Hormone replacement therapy (HRT) is often prescribed to women experiencing symptoms from the menopausal transition (eg, hot flashes, night sweats, uterine bleeding, mood changes, sleep disturbances, and sexual dysfunction). HRT can be administered orally or through use of transdermal patches or creams, and it can be estrogen-only or estrogen mixed with progesterone.^{29,31,32}

The effects of HRT on ocular surface dryness described in the clinical research literature are mixed. Some data indicate that HRT is helpful,

whereas other studies indicate that HRT is a risk factor for ocular surface dryness. The variability in the research is thought to come from differences in route and location of administration (topical vs oral, skin vs ocular), concentration levels, the use of placebo or nonplacebo controls, and the use of estrogen or estrogen plus progesterone. Further controlled prospective studies are required to determine the true impact of HRT on the ocular surface.^{1,31}

Although there are not enough data to recommend HRT as a treatment for menopausal or postmenopausal ocular surface dryness, eye care providers can counsel patients that HRT can potentially improve or worsen ocular surface dryness symptoms.

Because testosterone production also decreases during menopause, topical testosterone application has

been studied as a treatment for meibomian gland dysfunction. A phase 2 clinical trial by Schiffman et al demonstrated improvements in meibomian gland secretion and ocular comfort with application of 0.03% testosterone ophthalmic solution.³³ No studies past phase 2 have been initiated.

Should signs and symptoms of ocular surface dryness worsen during a patient's menopausal transition, it may be time to move from palliative therapies (artificial tears) to antiinflammatory interventions. These may include topical prescriptions such as cyclosporine ophthalmic emulsion 0.05% (Restasis, Allergan) or lifitegrast ophthalmic solution 5% (Xiidra, Novartis), amniotic membrane materials (membranes or drops), or autologous serum. A more frequent follow-up schedule or use of mechanical therapies for meibomian gland dysfunction may also be indicated.

WATCH YOUR PATIENTS' MILESTONES

Eye care practitioners should be aware that women's lifetime milestones of pregnancy and menopause can exacerbate or worsen signs and symptoms of ocular surface dryness. Patient intake forms and questionnaires can help doctors to pinpoint patients' relationships to these life shifts. Ocular surface dryness doesn't have to make these transitions more difficult. Modern therapies include new and updated options that can help patients at all stages of life. ■

AT A GLANCE

- ▶ The cornea, conjunctiva, and tear glands all have receptors specific to testosterone, estrogen, and progesterone.
- ▶ Ocular surface changes can occur anywhere throughout the 40 weeks of pregnancy but most commonly arise in the third trimester, when hormone levels are highest.
- ▶ During menopause, age-related decreases in DHEA and progesterone, combined with loss of hormones from the ovaries, has been correlated with worsening of ocular surface dryness signs and symptoms.

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