

Dry Eye: Awareness, Diagnosis, and Management

Why prevalence increases after menopause

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Dry eye is an ocular condition affecting approximately 10% to 20% of the population.¹ Its prevalence increases with age, and the majority of those affected are women—which is not surprising because evaporative dry eye and dysfunction of the meibomian glands often occur during aging and menopause.² In a recent study of 20 postmenopausal women, 13 subjects (65%) experienced symptoms of dry eye, and six of those women used eye drops to relieve symptoms.³

It is important for practicing clinicians to be aware of dry eye. Many patients depend on their general practitioner for all of their health needs, including ocular health. Dry eye greatly affects the patient's quality of life, so it is imperative for clinicians to be able to recognize the general signs and symptoms of the condition. This article will discuss the pathophysiology, causes, and management of dry eye. It will also review the manifestations and treatment of ocular allergy.

WHAT IS DRY EYE?

The ocular surface is protected from the external environment by the tear film. Although the tear film may seem like a simple boundary, it is actually quite

ABSTRACT: Dry eye is quite common in the population today, particularly among postmenopausal women. The condition greatly influences the patient's quality of life by causing significant ocular discomfort. Dry eye is characterized by many symptoms, including dryness, grittiness, and burning. Development of dry eye can be influenced by various factors, including autoimmune diseases, use of certain medications, and environmental conditions. Identification of contributing factors can help clinicians establish a course of treatment. One of the simplest ways to alleviate dry eye symptoms is with the use of artificial tears. Current research in the dry eye field shows a promising future for the development of effective treatments for the causes of the disease. (*Women Health Primary Care* 2004; 7(2):97-103)

complex. The tear film is composed of three separate layers: the lipid layer, the aqueous layer, and the mucin layer. The lipid layer forms the outermost layer of the tear film and is produced by the meibomian glands, which are located in the tissue of the eyelid. The lipid layer helps prevent evaporation of the tear film. The aqueous layer,

the thickest of the three, composes the middle of the tear film. It is produced by the lacrimal gland. The mucin layer is the innermost layer of the tear film. This layer contains mucins that are secreted from goblet cells, the lacrimal gland, and cells of the conjunctiva. Mucins help to form the glycocalyx that contributes to cell adhesion, allowing the tears to "stick" to the surface of the eye and make the tear film hydrophilic, so that the aqueous layer spreads evenly over the ocular surface.^{4,5} Each tear film layer plays an integral part in protecting the ocular surface; when a deficiency occurs in any of the layers, the tear film breaks down, exposing the ocular surface to the drying effects of the external environment.

SYMPTOMS

Dry eye is characterized by many symptoms, including dryness, grittiness, burning, foreign-body sensation, excess tearing, and sensitivity (Table 1). Patients may experience one or more of these symptoms. The excess tearing may seem counterintuitive, but it is a reflex

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response to the irritation and the foreign-body sensation that are caused by the dry eye.

Some patients also experience ocular itching that is caused by a combination of allergic and dry eye symptoms. These symptoms are often associated with each other, and dry eye may in fact exacerbate existing allergies. The tear film acts as a protective barrier against allergens and dilutes them before they reach the ocular surface. In dry eye, though, the tear film is deficient and allows the allergens to reach the ocular surface more easily, which causes mast cell degranulation and the onset of an allergic response. It is important to differentiate between dry eye and allergic symptoms (please see "Ocular allergy" on page 99), so that appropriate treatment can be selected. The hallmark symptom of ocular allergies is itching. In addition, ocular allergies are characterized by ocular redness (or "bloodshot eyes") (Figure 1), lid swelling, seasonality of symptoms (ie, symptoms coincide with elevated airborne pollen levels), the transient nature of symptoms (they come

Table 1. Symptoms of dry eye

- ◆ Dryness
- ◆ Grittiness
- ◆ Burning
- ◆ Foreign-body sensation
- ◆ Excess tearing

and go depending upon what the patient is being exposed to), and tearing (which makes the differentiation even more difficult).

DIAGNOSIS

Ophthalmologists can determine the presence of dry eye by using several tests. Checking the tear film break-up time is one way to evaluate the integrity of the tear film (Figure 2). Another approach is with conjunctival staining, in which fluorescein (a yellow dye) is instilled into the patient's eyes to reveal any cells damaged by drying.

A test that can easily be used in the primary care clinician's office or at home by the patient is the noninvasive method of checking the tear film break-up time. This test is performed by having the patient blink two times, and then timing to the first realization of ocular

awareness. This awareness is any change in ocular sensation that causes patients to focus more attention on their eyes. In this context, it can be characterized as dryness, burning, or any sensation that induces the need to blink. The presence of dry eye is suggested when ocular awareness occurs in less than seven seconds. (Tear film break-up time generally occurs within one second of ocular awareness.) This test can be used as a simple method for both clinicians and patients to monitor the signs of dry eye.

CAUSES OF DRY EYE OR SIMILAR SYMPTOMS

Many variables can influence the symptoms of dry eye, such as levels of circulating hormones, various autoimmune diseases, ocular surgeries such as PRK (photorefractive keratectomy) and LASIK (laser-assisted in situ keratomileusis), medications, environmental conditions, and visual tasking.

Circulating hormone levels decline during the aging process, particularly in women, because of the onset of menopause. Many theorize that this process is connected to the occurrence of dry eye in the following manner. Sex steroids stimulate the secretion of proteins from the meibomian glands, and with decreased levels of circulating hormones, fewer of these proteins are released. These proteins regulate the functional and secretory processes of the lacrimal gland, so lower levels of sex hormones can lead to decreases in production of the aqueous layer and impair the integrity of the tear film.⁶

Many autoimmune diseases, including Sjögren's syndrome and systemic lupus erythematosus, can be underlying causes of dry eye. Sjögren's syndrome is a chronic autoimmune disease characterized by loss of lacrimal and salivary gland secretions; dry eyes and dry mouth are the key manifestations.⁷ Sys-



Figure 1. A moderate ocular allergic reaction. Redness is common in ocular allergy but also in several other ocular conditions. When identifying ocular allergy, it is always important to ask patients whether they experience the hallmark symptom: itching.

Ocular allergy

Ocular allergy is a condition that for many reasons can elude a clinician's notice. Often, allergies may not be the primary reason for an office visit, and patients may not mention them, especially during the off-season. Patients who attempt self-medication with over-the-counter agents may not realize that more effective prescription agents are available. Integrating questions regarding allergy, including eye allergies, into patient questionnaires is easy and can improve patients' quality of life by allowing proper diagnosis and treatment.

Allergy and dry eye, two of the most common external ocular conditions, both can manifest with red, irritated eyes. However, they differ in at least two key respects. Patients with ocular allergy experience itching, while patients with dry eye usually feel burning or the sensation that there is a foreign body in the eye. The environment in which the patient's most severe symptoms occur can also help establish the diagnosis. Allergy is suggested by symptoms that flare outdoors during pollen seasons or indoors near pets, dust, or mold. Dry eye is suggested by discomfort that is exacerbated by dry conditions, such as forced air heating, wind, or dry heat, or by prolonged visual tasks.

In patients with ocular allergies, the mechanism of the allergic reaction begins when the mast cells, which are present in vast quantities on the conjunctiva of the eye, are triggered to degranulate by the arrival of an airborne allergen that has infiltrated the barrier of the tear film. The mast cells release a host of substances that cause the allergic reaction. The primary mediator released is histamine, which stimulates nerve endings to cause itching and blood vessels to cause redness and swelling. An interesting point is that mast cells are heterogeneous. This heterogeneity can be recognized in a variety of ways. Mast cells in different tissues have distinct cytokine profiles; this difference in cytokine profiles may help explain why we do not typically see a clinically significant eosinophil infiltration and late phase of reaction in the eye but do see this in other tissues.¹⁹ Mast cells found in various tissues and species can also vary in their reactivity to drugs. For example, mast cells in the human conjunctiva react differently to drugs than do those in other tissues or species. Therefore, the tissue or cell type on which preclinical and clinical research has been conducted is an important consideration when evaluating drugs.

MANAGEMENT

There are numerous effective options for the management of ocular allergy. Patient satisfaction and quality of life can be vastly improved by prescription agents that manage allergy and its hallmark symptom, itching, as well as its detrimental signs, such as redness and lid swelling.

The ocular symptoms of patients with allergy are sometimes overlooked in deference to their nasal complaints. A nasal spray alone, however, cannot aid the eyes.²⁰ In contrast, a prescription anti-allergy eye drop drains through the nose, helping to suppress the allergic reaction there.^{21,22}

Systemic antihistamines, including the new generation of agents, do not adequately treat the ocular component of allergy. In fact, they can have a detrimental drying effect on the tear film of the ocular surface.^{14,23} The deterioration of the tear film barrier makes the eye even more susceptible to entry by allergens. As a general rule, topical disease should be treated topically.

Most prescription anti-allergy eye drops are indicated for treatment of itching only, with the exception of olopatadine, which is indicated for treatment of all signs and symptoms. Lid swelling is a sign of allergy bothersome to many, although in the past it has gone unrecognized. Swollen, red eyes can detract from quality of life, and they can have negative social connotations by giving the appearance of tiredness or even substance abuse. Left untreated, lid swelling can become chronic, and structural microdamage can result from repeated stretching of the skin. In a recent study, lid swelling during allergic reaction was measured using scanning and imaging technology. Swelling was more than five times greater in untreated eyes than in those treated with topical ophthalmic eye drops (olopatadine 0.1%).²⁴

A proactive treatment strategy with topical, potent eye drops (even in the "off-season") can help patients to have control over itchy, red, swollen eyes when they occur. The cost benefit of using a powerful prescription allergy eye drop may be advantageous to patients as well. Since over-the-counter drops are short acting (two to four hours) and are indicated for administration four times daily, they may not maintain efficacy throughout an entire waking day. Stronger, multi-action prescription drops can provide day-long protection with fewer daily drops.

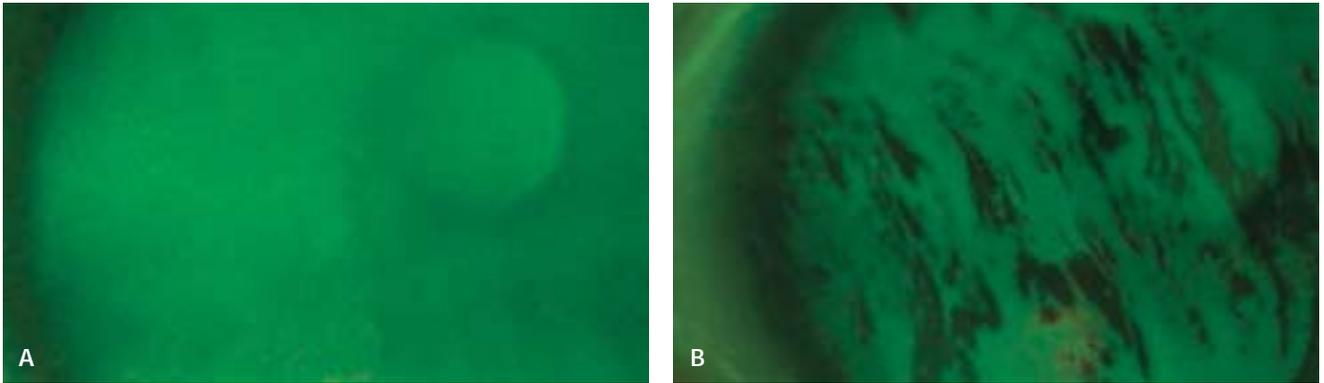


Figure 2. Tear film break-up time. This diagnostic tool measures the stability of the tear film. It is reliable and reproducible. Micro quantities of unpreserved sodium fluorescein are administered (A). When tear film break-up occurs (seen as black in a sea of green [B]), the ocular surface is exposed, resulting in dis-

comfort and the development of keratitis and redness. The same test can be performed without fluorescein by timing the patient's realization of ocular awareness, which indicates that the tear film is breaking up. Awareness within seven seconds suggests the presence of dry eye.

temic lupus erythematosus is a chronic, inflammatory, immunologic disease in which 7% to 54% of patients have dry eye.⁸ These and other autoimmune diseases present in various guises but often have ocular components.

Similarly, ocular surgeries can have an impact on the development of dry eye symptoms. For example, ocular dryness and irritation occur in more than half of LASIK patients.⁹ One study found that 13 of 19 patients (74%) experienced symptoms of dry eye up to six months after LASIK surgery.¹⁰ In this procedure, the nerves that run to the ocular surface are severed, which decreases corneal sensitivity and, in turn, secretions from the lacrimal gland, thus causing dry eye.¹¹

There are many medications that can influence dry eye symptoms by altering tear flow, tear production, or the composition of the natural tear film.¹² They include:

- ♦ Nonsteroidal anti-inflammatory drugs such as ibuprofen and naproxen.
- ♦ Tricyclic antidepressants and anti-anxiety agents, such as imipramine, doxepin, and amitriptyline.
- ♦ β -blocking agents such as metoprolol and propranolol.

As noted earlier, ocular allergies and dry eye symptoms can

occur simultaneously, and as a result many patients with dry eye symptoms use systemic antihistaminic medications. These agents, however, can exacerbate ocular dryness.¹³ Antihistamines act on the muscarinic receptors of the endocrine glands that regulate the secretion of fluid and protein in the eye. Both mucin production and tear production are greatly reduced by the antimuscarinic actions of antihistamines: Tear flow is decreased by nearly 50% in patients using oral antihistamines.¹⁴ Disruption of the tear film's composition greatly alters its stability, which can lead to the development of dry eye symptoms and ocular discomfort.¹³ Ocular allergies are more effectively treated with topical eye drops than with antihistamines.¹⁵ The topical medication provides direct relief of the ocular symptoms without influencing any other body systems and functions and, of particular importance, without drying the eyes.

Environmental factors can also affect dry eye symptoms. Low humidity, such as can be found in an arid climate or in a car with the defroster on, can exacerbate or induce dry eye symptoms. Finally, visual tasking can cause symptoms. Tasks that can greatly influence symptoms include watching televi-

sion or using a computer for long periods of time, which decrease the blink rate. When this rate is decreased, the tear film is replaced on the ocular surface less often, leaving the surface exposed to the external environment.

MANAGEMENT

One of the simplest ways to alleviate dry eye symptoms is with the use of artificial tears. There are many brands on the market, which allows patients to choose according to their needs. When used on a regular basis (eg, four times a day), eye drops can greatly decrease ocular discomfort. Dry eye is a chronic disease, and the available artificial tears manage the symptoms, but they do not cure the disease. Thus, dry eye patients will typically use eye drops year-round. The use may become more frequent in dry conditions, resulting in a seasonality of use—time periods during which use is heightened. A four-times-a-day dosing schedule may seem excessive to some, but it can help prevent ocular discomfort from developing and may be preferable to waiting for symptoms to occur. Many patients use a thick eye drop with a gel-like consistency. These drops provide long-lasting relief, but due to their high viscosity, they often blur vision for

several minutes, making them less practical for daytime use.

Warm compresses applied to the eyes for several minutes can improve ocular symptoms by stimulating the release of oily lipids from the meibomian glands. The oily lipids help to stabilize the tear film, thereby relieving some ocular discomfort.

Recently, some attempts to alleviate dry eye symptoms have focused on intake of essential fatty acids. Evening primrose oil has been investigated because it is a good source of γ -linolenic acid (GLA). Although GLA has alleviated dry eye symptoms in some patients, its role in eye health has not yet been defined.¹⁶ It is thought that GLA is a precursor needed to

form prostaglandin E1, which helps regulate functioning of the lacrimal gland. Thus, higher GLA intake may help improve lacrimal gland functioning and decrease dry eye symptoms.¹⁷ Furthermore, a study of 32,470 subjects from the Women's Health Study found that women with a higher intake of omega-3 fatty acids had a lower risk of developing dry eye (odds ratio, 0.83; CI, 0.7 to 0.98).¹⁸ These preliminary results form a promising basis for future investigations into the role of essential fatty acids in the development of dry eye.

NEW TREATMENTS

There are many new dry eye products currently being studied. They are designed to treat the physiologic

deficiencies underlying the signs and symptoms, rather than simply the immediate ocular discomfort. For example, secretagogues (eg, INS365) are designed to bind and stimulate the receptors responsible for secretion of the aqueous layer of the tear film in those patients who suffer from aqueous-deficient dry eye, or to stimulate the secretion of mucins. Another class of medications being investigated is the mucomimetics, which mimic the mucins that are present in the innermost mucin layer of the tear film. A third class of medications being investigated is that of immunosuppressive agents, including a cyclosporine ophthalmic emulsion that has been recently approved by the FDA. This product is thought to decrease ocular inflammation, thereby reducing the damage caused by the inflammatory response to the lacrimal gland. Lacrimation is thus decreased, reducing the signs and symptoms of dry eye. A recently marketed dry eye therapy (a solution containing demulcents, polyquad, and hydroxypropyl guar) is designed to help establish an environment conducive to the healing of the ocular surface. It creates a shield of protection on the surface by preferentially adhering to damaged epithelial cells, creating a scaffolding to protect the damaged cells from the external environment. These medications will provide more effective treatment of the underlying causes of dry eye.

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PRIMARY POINTS

Dry Eye

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There are many new dry eye products currently being studied. They are designed to treat the physiologic deficiencies underlying the signs and symptoms, rather than simply the immediate ocular discomfort.

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