

The dry eye

Dry eyes are a frequent problem, particularly in older people. The tear film is a complex structure with a superficial thin oily layer overlying the watery layer and then a mucous layer. Dry eyes are aggravated by drying conditions such as central heating or low blink rate, as seen when concentrating on television or driving. Many treatments are available for this condition and most can be purchased over the counter and self-administered by the patient.

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Dry eyes are a frequent problem, particularly in older people.¹ Minor degrees of the condition are very common and may go unrecognised since symptoms vary from minor irritation to severe discomfort. A patient complaining of sore eyes and blurred vision when performing a visual task may need attention to a dry eye condition, rather than a change in glasses.

The tear film² (figure 1) is very important to the wellbeing of the eye and to the maintenance of vision. The tear film, and not the cornea, is actually the main optical surface of the eye. Tears are produced throughout day

and night even when there is no particular demand and this is known as the resting rate of tear secretion. When demand is made on the tear glands, as occurs in eye irritation, then reflex secretion is brought into action.

The resting and reflex tear secretions have different anatomical sites of origin. The resting secretion comes largely from the accessory lacrimal glands, which are dotted around the conjunctival fornices and the reflex secretion comes from the lacrimal glands proper. The resting and reflex secretion processes can be interfered with differently by disease.

The tear film is quite a complex structure consisting of several separately identifiable layers. The most superficial of these is the thin oily layer which is secreted by the meibomian glands. The oily layer forms a barrier that is important in maintaining the stability of the tear film covering the cornea and conjunctiva and in preventing evaporation. The edge of the eye lid is also in an oily non-wettable condition and without this there

would be nothing to stop the tears running down our faces all the time.

The next layer from the surface is the watery layer of the tear film. This watery fluid contains various salts and proteins in solution and these are derived from the bloodstream through the process of secretion in the lacrimal glands. Thus, the tear film contains most of the constituents that are found in the blood plasma, but in a dilute form. Important amongst the proteins in the tear film are those that are concerned with

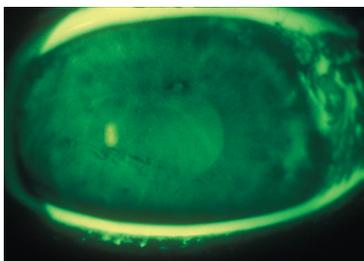


Figure 1: Normal tear film demonstrated by fluorescein

There is an even film over the cornea and well filled eyelid gutters



Figure 2: Breakdown of tear film

Fluorescein on a dry eye with a deficient film over the central cornea and punctate staining of the lower cornea and bulbar conjunctiva

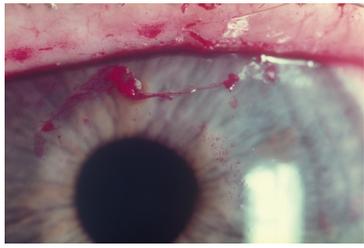


Figure 3: Excess mucus

Rose Bengal stain shows punctate staining of the cornea and of the adherent mucus

resistance to infection. One protein that is unique to the tear film is lysozyme, an enzyme that dissolves the protein coat of bacteria. The blood proteins concerned with resistance to infection are also present; the γ -immunoglobulins.

Under the watery layer of the tear film is the mucous layer, which forms the interface between the tear film and the cell surfaces of the corneal and conjunctival epithelia. The mucus content in this deepest layer is secreted by the goblet cells of the conjunctival epithelium and recently the epithelial cells themselves have been noted to secrete a mucus of their own.

The complex nature of the tear film, with the various different sources of origin of its several constituent parts makes it a delicate structure that is vulnerable to a variety of disturbances and the dry eye is not simply a matter of not having enough tear secretions. The



Figure 4: Meibomian gland dysfunction

Damage to the meibomian glands causes depletion of the oil layer of the tear film and breakdown of the tear film. Blocked glands are seen in the upper lid margin.

lysozyme content is particularly liable to be an early casualty in dry eye, increasing the risk of infection.

Breakdown of the tear film leads to damage to the conjunctival and corneal epithelia with loss of epithelial cells leading to little pits which show punctate staining with fluorescein (figure 2). Mucus may be produced excessively and tends to adhere to the surface (figure 3).

The oily layer is synthesised in the meibomian glands from essential fatty acids. Lack of the oily layer is consequential to meibomian gland dysfunction (figure 4). The lid margins are constantly in contact with the skin bacterial flora and this can lead to blepharitis. Meibomitis is often a component feature of blepharitis and this can result in the destruction of some or many

of the meibomian glands with a permanently adverse effect on the tear film.

Aggravating conditions

The patient's history will often give a clue to the diagnosis of dry eyes. Certain activities and environments tend to aggravate the symptoms by accelerating the evaporation of the tear film. Patients with a low blink rate tend to suffer more. This appears to be the natural state of some individuals and also occurs in Parkinsonism.

A blink usually accompanies a change of gaze direction in activities that involve looking around, but blinking can be

infrequent when the gaze is concentrated in one direction. People tend to blink very little when concentrating on the road ahead whilst driving, particularly on the motorway, which requires very little change in gaze. Television too produces the no blink situation.

Patients can help themselves a little by deliberate blinking, or by stopping their activity to rest with their eyes closed. The British climate is never very hot and the humidity usually remains relatively high. Hot dusty climates, near to the equator can be quite irritating to dry eyes. In Britain, mainly indoor environments present problems.

Tear film evaporation is

Box 1: Drugs associated with dry eyes**Antihistamines**

Acrivastine

Cetirizine

Antihypertensives

Quinapril

Hydrochlorothiazide

Antiemetics

Prochlorperazine

Dramamine

Antidepressants

Citalopram

Doxepin

Diuretics

Triamterene

Hydrochlorothiazide

Cytotoxic

Methotrexate

 β -blockers

Atenolol

Metoprolol

Propranolol

Carvedilol

Amlodipine

Alcohol

aggravated by a source of dry heat such as a gas or electric fire near the patient and with central heating or air conditioning. Car heaters are a particular nuisance since dry warm air can be blown towards the driver's eyes.

Several commonly used drugs have a tendency to cause or to aggravate dry eyes, particularly antihistamines, parasympathetics, antidepressants, and diuretics (box 1).¹ In some instances this is due to a direct pharmacological effect on tear secretion, as in parasympathetics.

Presentation

Patients with dry eyes can present with very variable symptoms, which can be quite misleading. Typically, the patient gradually develops eye irritation and redness, with symptoms aggravated by drying conditions. They may also have had episodes of conjunctivitis in which infection has played a part.

Patients who present with eye watering and may have an overflow of tears can have dry eyes. This apparent paradox is explained by the different effects that the dry-eye condition has on the resting and reflex tear secretions. The resting secretion is diminished, leading to a dry eye and symptoms of irritation. This irritation then produces reflex tear secretion and the eye may water.

Causes of reduced tear secretion

By far the most common cause of dry eyes in the UK is a spontaneous reduction in tear production in ageing individuals. The dry eye may be secondary to destructive disease of the conjunctiva or the lacrimal glands. Permanent damage to the conjunctiva follows some inflammatory diseases, of which the most common worldwide is trachoma.

Vitamin A deficiency, which is seldom seen in Britain, leads to a dry eye condition with conjunctival changes that make it unwettable (figure 5). Destructive disease of the lacrimal glands is most usually due to inflammation. The best

known condition of this type is Sjögren's syndrome, which should be considered in patients with dry eyes and arthritis.

Treatment

Mild cases need little more than the advice to avoid drying circumstances and to interrupt visual activities with blinking or resting with the eyes closed for short periods.

Ocular lubricants

Many products are available without prescription for treating the dry eye. These include eye drops, gels, eye ointments and lubricant eye sprays. The eye-drops give relief for a relatively short period of time. The original eye-drops for dry eyes were based on methyl cellulose solutions, which are short-acting.

Eye-drop manufacturers have introduced drops with longer chain molecules that persist better in the tear film, beginning with hydroxypropyl methyl cellulose (hypromellose), and more recently with greater effectiveness, polyvinyl alcohol and sodium hyaluronate. Carbomer gels are longer acting

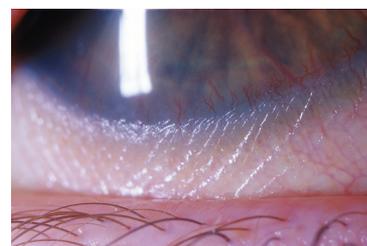


Figure 5: Vitamin A deficiency

Non-wettable conjunctiva of severe dry eye

Box 2: Essential fatty acids**Omega-3**

α -linolenic acid

Eicosapentanoic acid

Docosahexaenoic acids

Omega-6

γ -linolenic acid

Linoleic acid

Arachidonic acid

than liquid drops, but they do make the vision blurred. Hydroxypropyl guar drops have the advantage of turning from a liquid to a gel once in the eye.

These lubricating eye-drops supplement the aqueous layer of the tear film, but do not help the oily layer. The oily layer can be supplemented with a paraffin ointment, which is best used before bed because the vision is made smeary.

Liposic eye gel contains both a carbomer gel and an lipid lubricant and has less adverse effect on vision. A phospholipid-based mist spray assists (Eye Logic, formerly Clarymist) the oily layer without affecting vision and in my experience, it is well accepted by patients. A new spray containing liposomes (Actimist) that is applied to closed eyes was introduced in 2008 but has little clinical experience.

Patients whose symptoms are not adequately improved by a tear supplement should consider adding an oil supplement. Eye lubricants are not classified as prescription-only medications and a patient can obtain them directly in a pharmacy. Frequent use of eye drops and gels can lead

to reactions to the preservative, which is benzalkonium chloride in most cases. Once sensitised, the patient's symptoms become worse on further application.

Preservative-free eye drops are largely confined to one-shot plastic ampoules, of which several are available, but Hycosan, a hyaluronate without preservative, and Oxyal, a hyaluronate with a biodegradable preservative have recently been introduced.

Nutritional management

About 50 essential nutrients are known, including vitamins, minerals, carotenoids, and essential fatty acids. Early research concentrated on the role of vitamins, but recently the important role of carotenoids and of the essential fatty acids has been recognised.³ The essential fatty acids are so named because the body cannot synthesise them, so the fatty acid, or its precursor is needed in the diet. Essential fatty acids are the omega-3 (ω 3) and omega-6 (ω 6) polyunsaturated fatty acids. Omega-3 is characteristic of fish oil and omega-6 of plants, such as the evening primrose.

The health value of omega-6 evening primrose oil has become established in ocular health and in a number of conditions not directly related to the eye. More recently, the role of omega-6 fatty acids has been recognised as essential to ocular health, particularly for dry eyes⁴ and blepharitis.⁵

The way in which essential fatty acids benefit ocular health are many and the biochemistry is

often complex. They regulate cell membrane function and serve as precursors in the formation of the inflammatory mediators, prostaglandins, leukotrienes and thromboxanes.⁶ Thus the essential fatty acids are seen as having a role in modifying or reducing inflammatory processes.

Omega-3 and omega-6 are not single substances, but each comprises a group of essential fatty acids with similar characteristics (box 2). Beneficial effects of an evening primrose oil supplement have been reported in dry eye.⁷ In dry eye due to Sjögren's syndrome, there is theoretical and practical evidence of a therapeutic effect.^{8,9} Patients with Sjögren's syndrome have high levels of circulating prostaglandins coupled with depletion of the prostaglandin precursors dihomo- γ -linolenic acid and arachidonic acid. A supplement of essential fatty acids might therefore be beneficial and a placebo-controlled trial has confirmed this.⁸

Essential fatty acids for dry eyes

Omega-3 promotes tear production by inhibiting both inflammation and lacrimal gland cell death. In dry-eye conditions due to diminished tear production, such as in Sjögren's syndrome, inflammatory cytokines cause inflammation, which has the effect of inhibiting tear secretion.⁹ Omega-3 gives benefit by the anti-inflammatory effect of prostaglandin E3, which is synthesised from Omega-3,¹⁰ and is able to combat the cytokine effect.

In dry eyes there is also

increased apoptosis of cells in the tear glands due to the activity of tumour necrosis factor (TNF)- α . The loss of cells leads directly to diminished tear production. The action of TNF- α is suppressed by the omega-3 fatty acid, eicosapentanoic acid, with reduction in the rate of loss of cells and better maintenance of tear production.

The tear film oil is synthesised in the meibomian glands from essential fatty acids and evidence suggests that essential fatty acid intake can alter the lipid profiles of meibomian gland secretion,⁸ which may produce a more efficacious oil. Thinning of the oil has been recorded and this may promote better flow from the gland.

Essential fatty acid supplements are also considered to have a significant role in the management of blepharitis⁵ and thus in maintaining functional meibomian glands. The beneficial effect of essential fatty acids and in particular of the omega-3 fatty acids in the management of blepharitis is likely to be in reducing inflammation and in modifying and increasing the meibomian gland secretion.

Omega-3 derived prostaglandin E3 suppresses the inflammation of blepharitis. Patients with ocular surface disease, such as dry eye and blepharitis should be encouraged to eat a diet rich in fish and vegetables. Omega-6 supplements are available from pharmacies and health food shops as evening primrose oil and as star flower oil. Omega 3 capsules are derived from fish or from flax seed. The capsules commonly contain added vitamin E which acts as

an antioxidant to preserve the capsule contents and is also relevant to the patient because the long-term supplementation of essential fatty acids produce free radicals which deplete the body's vitamin E reserve. There is no recommended daily allowance (RDA) figures for essential fatty acids,¹¹ but some suggest that an adult's diet should contain 0.65 g of omega-3 and 2.8 g of omega-6.¹²

Management of severely dry eyes

Severely dry eyes present significant problems. One simple surgical measure is closure of the lower lacrimal puncta to prevent loss of tears by their normal drainage route. This operation carries the occasional risk of tear overflow, so preceding surgery with a reversible closure with lacrimal plugs is advisable. Overall, providers of primary eye care can do much for patients with dry eye in identification and management of the condition.

I have no conflict of interest.

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