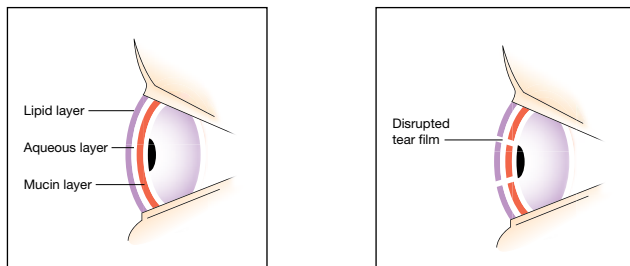


## Treatment of dry eyes

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In healthy eyes, the tears form a moist film over the surface and protect the cornea and conjunctiva from dehydration. In Sjögren's Syndrome an immune attack on the lacrimal glands and conjunctiva reduces the volume and quality of the tears and causes the eyes to become dry.

### The structure of the tear film



Healthy eye

Dry eye

The normal tear film has three layers:

- The deepest is a mucous layer called Mucin. This maintains lubrication of the lids during blinking and eye movements.
- The second layer provides a watery fluid, which keeps the surface of the eye moist and provides protection from infection through the presence of several defence proteins. When the eyes are open, tears are produced by the lacrimal glands in response to sensory inputs from the surface of the eye and other parts of the body. Emotional events, or irritants such as smoke, onion vapour or the presence of a foreign body in the eye, can stimulate an immediate and more copious secretion of tears.
- The third layer is an oily layer present at the surface of the tear film which conserves tear water by reducing evaporation. Tear oil is produced by the small, Meibomian glands of the eyelids. The presence of meibomian oil along the lid margins also prevents tear overflow.

### Some features of dry eye

In Sjögren's Syndrome there is principally a shortage of the watery, lacrimal component of the tears (or second layer) but a disturbance of each of the tear film layers may occur. Symptoms arise from poor wetting and lubrication of the eye surface, injury to the surface cells of the eyeball because of increased friction and the release of inflammatory mediators.

### Factors affecting severity of symptoms

The symptoms of dry eye vary from day to day, depending on environmental factors and the physical state of health. In terms of the environment, low humidity encourages water loss and symptoms are worse in air-conditioned rooms, on hot sunny

### The basis of dry eye symptoms

- Reduced tear volume due to lacrimal gland failure
- Reduced tear lubrication (increased friction) between the eyelids and the globe
- Surface damage to nerve endings at the surface of the eyeball
- Release of inflammatory chemicals into the tears
- Increased salt concentration (hyperosmolarity) due to reduced tear volume or increased evaporation from the tear film. Increased evaporation can be caused by a deficiency of the lid oil (meibomian oil).

### Ocular symptoms of dry eye

- Grittiness – foreign body sensation
- Burning
- Light sensitivity
- Mild ocular redness
- Blurred vision
- Tired eyes – difficulty keeping the eyes open
- Mucus discharge – long strands of mucus can attach to the corneal surface as filaments and cause a painful filamentary keratitis. Very occasionally irritation of the eyes may stimulate episodes of watering, but this is rare.

dry days or dry frosty days. Symptoms are greatly exacerbated by smoky or dusty atmospheres. Room humidifiers and plenty of broad-leaved plants can help to achieve more humid indoor conditions. Some occupations can influence dryness too; working at a computer screen causes the eyes to be held more widely open and results in greater evaporation from the eye. Placing the terminal at a lower level, so that the eyes are directed downwards, can help reduce this effect.

Certain medications, used in the treatment of allergy, high blood pressure and gastro-intestinal disorders, may reduce tear secretion. Antihistamines and some travel sickness pills may reduce tear secretion and should be avoided where possible, by people who have dry eyes.

An area of uncertainty is the influence of sex hormone levels on lacrimal gland function. There is evidence that a deficiency of circulating androgens may trigger inflammatory changes in the lacrimal glands, which may explain the onset of dry eye symptoms around the menopause. For this reason androgen containing drops are under consideration for the treatment of dry eye. There are reports too, at least in the general population, that HRTs, particularly those containing oestrogens, may favour the occurrence of dry eye symptoms.

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### Trigger factors which increase dry eye symptoms or severity

Trigger	How does it act?	Examples
Low environmental humidity	Encourages tear evaporation	Air-conditioning Air travel Dry climate
Air-pollution	The dry eye is less able to clear irritant chemicals	Smokey rooms Dusty office Environments
Eyes more wide open than usual	The wider open the eyes are, the greater the surface evaporation	Working at a video display unit Playing Snooker Prominent eyes from thyroid disease
Infrequent blinking		Reading Looking through a microscope Walking round a supermarket Sewing
Certain medications*	They can sometimes reduce tear secretions	Blood pressure pills Allergy preparations Travel sickness pills Anti-spasmodics for stomach cramps or period pains HRT therapy

\*Consult your doctor or pharmacist if concerned about this

### Standard diagnostic tests for dry eyes

Test	How is it done?	Dry eye is suggested by:
A questionnaire about symptoms.	Some simple questions are asked.	Certain typical symptoms.
The tear film break-up test (BUT)	The tear film is dyed green with a small drop of fluorescein dye.	A short break-up time. (This is a test of tear film stability).
Ocular surface staining.	Fluorescein, or other dyes are instilled into the eye.	Uptake of the dye by the ocular surface in a particular pattern. More staining indicates greater severity of disease.
The Schirmer test.	Filter paper strips are hooked around each lid margin.	A reduced length of wetting of the strip. The test is an indicator of the reflex tear response.
Oil gland function.	Gentle pressure is applied to the lids to check oil expressibility.	An extensive lack of expressible lid oil.

### Special tests\*

Lacrimal tear proteins: e.g. Lactoferrin	Tears are collected and assayed. This can be done with a disposable unit.	A low tear concentration of lactoferrin. It indicates a loss of functional lacrimal tissue.
Tear osmolarity (depends on salt concentration)	A tiny drop of tears is placed into a measuring unit.	A raised tear salt concentration.

\*These tests are not currently available in general clinics

### Tests and Diagnosis

Diagnosis of dry eye is based on a small number of tests carried out in the clinic.

The patient may be asked to complete a questionnaire establish whether the typical symptoms of dry eye are present. Reduced tear stability, which is typical of dry eye, can be detected by staining the tear film with fluorescein dye. An early break-up of the stained film is indicative of drying. This dye can also be used to show if there is ocular surface damage. The dye is taken up by the damaged surface and the amount of damage can be graded as an index of severity. In the Schirmer test, which is a test of reflex tear flow, the ends of two filter paper strips are hooked over each lower lid and allowed to absorb tears for 5 minutes, with the eyes closed. A reduced amount of wetting is suggestive of dry eye. This is an uncomfortable test but need not be repeated frequently.

Other tests are available but are not routine such as estimating the increase in tear salt concentration in dry eye by measuring tear osmolarity, or measure the loss of the tear lacrimal protein, lactoferrin which indicates decreased lacrimal function. Some patients with Sjögren's Syndrome may also have Meibomian gland disease, which contributes to dry eye by increasing water loss from the eye. This can be diagnosed by clinical observation.

### A stepwise approach to treatment

**Stage 1 - Mild symptoms:** These can often be managed simply, with preserved tear substitutes bought without prescription at a low cost (e.g Hypromellose) and used as required, say 3-4 times a day. If such an approach fails then it is reasonable to try alternative preserved drops, since tolerance to specific preparations varies from patient to patient. This may require a doctor's prescription. If a drop is well tolerated then drop frequency can be increased to respond to an increase in symptoms.

**Stage 2 – Moderate symptoms or a poor response to therapy:** If stage one fails or the required drop frequency has risen to over six times daily, then it is worth considering a switch to an unpreserved, unit dose preparation. These preparations have greater convenience in use, but they are more expensive than preserved preparations. Alternatively, the use of a gel preparation may allow the frequency of instillation to be reduced.

**Stage 3 – Severe symptoms:** Patients with severe dry eye may be helped by introducing punctal plugs or by permanent punctal occlusion and by the provision of moisture-conserving spectacles.

### What treatments are available?

There are several approaches to the treatment of dry eye and severe dry eye may require a combination of measure.

### Tear substitutes – artificial tears

Tear substitutes are dropped into the eye to improve wetting of the ocular surface. Most formulations contain a viscous polymer, such as hypromellose, this prolongs the length of time in the tear sac and reduces reapplication of the drops, since high viscosity in these drops they can cause visual blurring and a sense of viscous drag during blinking. Some polymers, have a property which makes the viscosity to reduce during the blink ('shear thinning ') so that the drop is better tolerated. Other viscous polymers which have this property are the carbapols, which are contained in gel preparations such as Geltears® and Viscotears®.

### Mucolytics

Where abnormally thick strands of mucus or adherent filaments

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are particularly problematic, drops that break down the mucus (acetylcysteine - Ilube®) may be of use, though they sting a little and have a sulphurous smell. They are usually prescribed after frequent use of standard artificial tears has failed to eliminate the problem.

### Summary of treatments for dry eye (topical agents unless otherwise stated)

#### Tear Substitutes:

Newtonian (Hypromellose)  
Non-Newtonian (Hyaluronic acid) Systane®

**Non-Preserved Drops:** Unit dose

**Ointments:** Simple eye ointment

#### Special Agents:

Mucolytics  
Acetyl cysteine (Ilube®)

#### Anti-inflammatories:

Steroids  
Cyclosporin – A – (Restasis®)

**Tear Stimulants:** Oral pilocarpine

#### Tear Conservation:

Punctal plugs or occlusion  
Moisture-preserving spectacles

**Dietary measures:** Fish and flax seed oils  
(containing omega-3 fatty acids)

#### Environmental measures:

Ensuring a less dry work and home environment.  
Adjusting behaviour – e.g lowering the level of the computer screen

#### General medical measures:

Where possible, avoid medicines which dry up tear secretions.

## Drops containing preservatives

The majority of tear substitutes contain a preservative, which enables the drops to be used for one month after opening the container. Preservatives inhibit the growth of bacterial contaminants that enter the opened bottle. Preserved drops are suitable for the majority of dry eye sufferers. Usually the simplest form of tear substitute is selected by the physician and changes of therapy made according to the response. The most commonly prescribed drop is Hypromellose, which is available over the counter at the chemist, it is a preserved drop and other similar drops are made commercially. Not all preserved preparations contain the same formulation or preservative, so it is worth trying different preparations to find which one gives comfort for the longest time.

## Preservative-free drops

In some patients, preservatives, such as benzalkonium chloride, cause an allergic or toxic response. Toxicity is most likely when drops have to be used frequently for severe symptoms and may give rise to signs of increased inflammation. Where this is suspected, treatment should be switched to the use of a preservative-free preparation. These are available commercially in 'unit dose' vials of sterile drops which are opened when needed, instilled into each eye and then discarded. They are available on prescription, but some are available over the counter. They are expensive and therefore not used for every patient, but in a sensitive individual, or in severe disease, they have the great advantage of safety and convenience in use.

Preservative-free drops may sometimes also be made up especially by a hospital pharmacy, on the instruction of a physician. These preparations are supplied in standard dropper bottles, which may be used for one week only. Beyond this time there is a risk of bacterial contamination.

## Frequency of drops

Drops are used to provide comfort for the eye and should be instilled as frequently as necessary to achieve this. This can be as little as four times a day or as frequently as every hour, according to the severity of symptoms. If symptoms persist, this may mean that they need to be used more frequently or alternatively that a different drop should be tried.

## Ointments

Some patients find that simple lubricant ointments, used at night, can be helpful where symptoms are not controlled by frequent use of drops. This may cause stickiness and misty vision in the morning.

## Steroid drops

Short courses of steroid drops are recommended to damp down inflammatory episodes in dry eye patients. They must be used with caution and under ophthalmic supervision to avoid the risk of steroid complications.

A wide range of tear substitutes is available worldwide, although many are not available in the UK. Occasionally, when there are good indications, such preparations can be obtained by special arrangement with the drug company concerned and used under the supervision of your doctor.

## Systemic therapy (oral medication)

In some patients with Sjögren's Syndrome, the salivary and lacrimal glands possess functional tissue which does not respond to normal reflex nervous stimulation. In these cases it may be possible to stimulate secretion by the use of oral pilocarpine and related agents, which can stimulate the natural receptors of the glands. Because pilocarpine has other effects on the body, the dose must be built up slowly over a period of time. Side effects include sweating, stomach cramps and diarrhoea, but in many patients treatment is well tolerated and successful.

## Dietary measures

Certain necessary dietary fats, termed 'essential fatty acids' can only be supplied in the diet, since they cannot be manufactured by the body. The omega-3 fatty acids, contained in flax seed oil and fish oils, are an example. They are metabolized in the body to anti-inflammatory products, which may have a beneficial effect in dry eye patients. There is evidence that dry eye symptoms are less frequent in patients with a higher dietary intake of omega-3 fatty acids. Omega-3 fatty acids are found in natural foods but are also available as dietary supplements.

## Conservation of tears

A further approach to the lack of tears is to conserve tear fluid that is still available. This is achieved by blocking tear drainage or reducing evaporation.

## Blocking tear drainage

Tears leave the tear sacs by fine canaliculi to reach the nose. The entrances to these canals are the puncta. Therapeutic blocking of the puncta conserves available tears and makes better use of instilled drops. A range of tiny plugs is available which can be inserted into the puncta after a drop of local anaesthetic. These are made of silicone rubber or another polymer.

A typical plug is mushroom shaped and when in place forms a cap over the punctum which prevents tears from leaving the sac. Different sizes of plug allow the best fit to be achieved. Plugs can remain in place for many months and if they come out, can readily be replaced. If they produce an important improvement in symptoms then it may be useful to arrange for a permanent, cautery or laser occlusion of the puncta, under a local anaesthetic.

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## Treatments for dry eyes

Product	Preservative free	Notes		Prescription or over the counter
Celluvisc 0.5%	Yes		Single dispensers	Prescription
Celluvisc 1%	Yes		Single dispensers	Prescription
Systane	No	polyquad-c		
Artelac	Yes	hypromellose 0.32%		Prescription
Hyco-San	Yes	sodium hyaluronate 0.1%		Over the counter
Vismed	Yes	sodium hyaluronate 0.18%	Single dispensers	Prescription
Refresh	Yes		Single dispensers	Over the counter
Blink	Yes		Single dispensers	Over the counter
Clarymist			Spray	Over the counter
Lacri-lube			Ointment	Prescription

## Reducing evaporation

Evaporation can be greatly reduced by providing a more humid environment around the eye. This can be achieved with moisture-conserving spectacles, which provide snugly fitting side shields which are attached to the spectacle frame. These are available commercially or can be made up by the hospital optometry department or by your local optician. The moisturizing effect of these spectacles can be enhanced by gluing small sponges onto the inside of the frames and wetting these from time to time. Many patients are helped by these spectacles, but occasionally the excess moisture causes misting up of the spectacle lenses and some patients find the appearance of the spectacles cosmetically unacceptable.

## Conclusions

In general, dry eye symptoms are more severe in Sjögren's Syndrome than in non-Sjögren's Syndrome dry eye. It reflects a greater degree of lacrimal damage and also a greater frequency of associated oil gland obstruction, which exacerbates the dry eye state.

There is a constant search for new medications and approaches to the treatment of dry eye. Because of the needs for thorough testing, it takes many years for these preparations and devices to reach the public, but progress is being made and the range of treatments and possibilities for relieving dry eye symptoms are steadily improving.