Dry eyes

Synonyms: dry eye syndrome, dysfunctional tear syndrome, keratoconjunctivitis sicca, xerophthalmia (used for dry eye associated with vitamin A deficiency)

Tears are a complex solution of water, proteins, salts, lipids and mucins. These play a hydrating, immunological, nourishing and lubricating role. Some of the components are simply there to allow the tears to remain on the corneal surface effectively and the tear/cornea interface has important refractive properties. The tears are produced under nervous and hormonal control by various glands within the eyelids and adjacent to the globe, the biggest of which is the lacrimal gland. Each type is responsible for producing a different combination of the components essential to good tear maintenance. The lacrimal glands produce the water, salts and proteins; the meibomian glands produce the lipids, and conjunctival goblet cells produce the mucins. The lids and blink reflexes are equally important in distributing the tears across the corneal surface.

Epidemiology

Dry eye syndrome is a common condition affecting 15-33% of those aged over 65 years. Prevalence increases with age. It is 50% more common in women than in men.

Aetiology

Dry eyes can arise as a result of insufficient tear production, excess tear loss, abnormalities of eyelids and blinking, or changes in tear film composition. Different forms of dry eye interact with each other, creating a vicious circle. Inflammation is both a cause and a consequence of dry eye, and can have a key role in maintaining the vicious circle. The inflammation does not necessarily manifest as redness. Preservatives found in artificial tears (particularly benzalkonium chloride) also contribute to the problem.

Aetiological classification for dry eye [1] [2]

Hyposecretive (aqueous-deficient or tear-deficient) causes	Evaporative causes
1. Sjögren's syndrome Primary - no associated connective tissue disease. Autoimmune disease affects lacrimal and salivary glands. Secondary - associated with other autoimmune connective tissue disease (eg, rheumatoid arthritis and systemic lupus erythematosus). **2. Non-Sjögren's syndrome** *Lacrimal gland insufficiency:* Age-related. Congenital. Infiltrative process (eg, lymphoma, sarcoidosis, AIDS, graft-vs-host disease). Lacrimal gland ablation or denervation. *Lacrimal gland obstruction:* Trachoma. Burns. Erythema multiforme. *Reflex hyposecretion (sensory block causing loss of corneal sensation):* Diabetes. Contact lens wear. Corneal surgery. Herpes zoster opthalmicus. Herpes simplex keratitis. *Reflex hyposecretion (motor block):* Cranial nerve VII damage. Anticholinergic medication. *Medication causing hyposecretion:* Antihistamines. Antidepressants (tricyclic and selective serotonin reuptake inhibitor). Diuretics. Beta-blockers. Antispasmodics.	**1. Intrinsic** *Meibomian gland dysfunction (reduces lipids in tear film):* Blepharitis. Systemic dermatoses (eg, rosacea or seborrhoeic dermatitis). Drugs (eg, isotretinoin). *Blink disorders - such as:* Parkinson's disease. *Lagophthalmos (inability to cover the eyes completely when closing the eyelids) - such as:* Thyroid ophthalmopathy. **2. Extrinsic** Vitamin A deficiency. Preservatives in topical drops. Contact lens wear. Ocular surface disease (eg, allergic conjunctivitis).

Common causes in general practice

Most people with dry eyes have no measurable abnormality of tear production, and no serious disease affecting tear composition. Common causes are:

- Decreased tear production, commonly due to:
    - Blepharitis - eg, from seborrhoeic dermatitis, atopic dermatitis, or rosacea.
    - Adverse effect of drugs.
    - Allergic conjunctivitis.
- Increased evaporation of tears due to:
    - Low humidity - from central heating, air conditioning or high wind conditions.
    - Low blink rate, wide lid aperture - eg, from prolonged use of a computer or microscope.
    - Allergic conjunctivitis.

The more common systemic causes to consider in general practice are endocrine (thyroid disease, diabetes), medication (antihistamines and antidepressants), Parkinson's disease, and rosacea [3] .

Contributing factors [4]

Risk factors for dry eye include:

- Female gender.
- Older age.
- Diet low in omega-3 essential fatty acids (or low ratio of omega 3 to omega 6).
- Postmenopausal oestrogen therapy
- Low-humidity environments, computer use or prolonged reading, smoking, vehicle pollution.
- Refractive surgery and use of contact lenses.

- Vitamin A deficiency
- Malignant tumours (due to radiotherapy and systemic chemotherapy).

Presentation

Symptoms

The diagnosis is usually made on the history:

- Gritty irritation and foreign body sensation.
- Burning or mild pain, aggravated by air conditioning, prolonged reading or computer work, dry air, etc.

Symptoms tend to be worse towards the end of the day. If symptoms are worse on wakening, with red and sticky eyelids, this is suggestive of dry eye syndrome caused by meibomian gland dysfunction.

Less often, there may be itching, photophobia and a tired or heavy feeling. Some patients may report a lack of emotional tears or may have noticed a less vigorous response when peeling onions. Some patients paradoxically complain of too much tearing - an excessive reflex response to corneal dryness. There may be excessive watering of the eyes in windy conditions.

Signs [3]

- The eyes are usually normal on examination, or there may be mild conjunctival redness.
- If severe, there may be signs of complications - eg, conjunctivitis or corneal ulcer.
- Look for signs which may indicate potential causes: local eye disease, skin disease, goitre, Parkinsonian signs, joint inflammation or deformity.

Assessment

- How troublesome are the symptoms?
- Is there any corneal damage?

- Is there any other explanation for these symptoms and signs? (See 'Differential diagnosis', below.)
- Is there any underlying cause for the dry eye? (See above list.)
- What treatment has already been tried?
- Are there any aggravating or risk factors?

Severity can be formally graded (usually in secondary care) by use of symptom questionnaire, tear break-up time test and examination of cornea (see 'Investigations and diagnosis', below) [2] .

Red flags [3]

- Moderate-to-severe eye pain.
- Persistent or significant visual loss.
- Photophobia.
- Marked redness of one eye.
- Diplopia.
- Acute onset.
- Signs of systemic ill health such as weight loss or fever.

These findings should prompt urgent referral.

Investigations and diagnosis [4]

Formal diagnosis, when required, involves tests not usually performed in a primary care setting. This will require referral to a community optometrist or ophthalmologist . Tests which are used include:

- Slit-lamp examination.
- Tear break-up time.
- Schirmer's test.
- Assessment of corneal damage, by staining with dyes - eg, rose Bengal, lissamine green or fluorescein.

- Symptom questionnaires. These assist in grading the severity of dry eyes.

Investigations for underlying causes (eg, TFTs, serology for circulating auto-antibodies) may be indicated.

Tear break-up time

This simple test needs the use of a slit lamp, set on a bright-light setting with a cobalt blue filter.

- Instil fluorescein into the lower fornix.
- Ask the patient to blink several times and then stop.
- Measure the time between the last blink and the first appearance of a dark spot on the cornea (formation of a dry area).

A tear break-up time of <10 seconds suggests dry eyes.

Schirmer's test

- Instil a drop of local anaesthetic (optional).
- Prepare a filter paper (5 mm x 35 mm with folded end).
- Gently dry the eye.
- Apply the filter paper with the folded end hooked on to the lower lid margin at the junction between the middle and outer third (take care not to touch the cornea).
- Tell the patient to keep their eye open and to blink normally.
- Measure the amount of wetting after five minutes: wetting of <5 mm (without anaesthetic) indicates dry eye.
- Protect the eye if local anaesthetic was used.

Differential diagnosis

- Other causes of an acute painful red eye - see the separate article. Conditions include keratitis, iritis, acute glaucoma and episcleritis. Dry eyes tend to be a bilateral condition, even if one eye is more affected than the other.

- Conjunctivitis - allergic, infective, or irritation.
- Blocked lacrimal duct.
- Blepharitis - this often co-exists with a degree of dry eye, and may be a cause.

Treatment aims

- To ease discomfort.
- To protect and preserve the cornea.
- To treat any underlying conditions.

Referral

- **Same-day referral** if the symptoms are severe or the cause diagnosis is uncertain - eg, pain more than mild, marked redness, photophobia, acute onset, unilateral symptoms/signs or visual acuity reduced.
- If symptoms are uncontrolled despite about four weeks of adequate treatment (the patient reliably taking their drops and trying to minimise risk factors).
- If diagnosis requires specialist assessment. (Self-referral to an optometrist may be appropriate in some cases.)
- If vision deteriorates or the cornea is affected.
- For underlying disease.

Management

Initial management in primary care - mild disease[3]

- Explain the protracted nature of this condition and the importance of the patient's input in managing it.
- There may be concurrent blepharitis and good lid hygiene measures can go some way towards alleviating both problems (see the separate Blepharitis article).

- Reduce aggravating factors:
    - Review medication.
    - Reduce cigarette smoking or second-hand smoke.
    - Avoid draughts (use shields if necessary) and low humidity (humidifiers can help).
    - Take regular breaks from computer work, TV and reading, which are associated with reduced blinking[4] . Lowering the computer screen to below eye level can decrease lid aperture.
    - Minimise contact lens wear. Consider silicone-hydrogel or rigid gas-permeable lenses if they must be worn.
- Treat underlying conditions - eg, allergies, dermatoses.
- Tear substitutes - drops, gels and ointments (see box). This is the mainstay of treatment. The choice depends on patient preference and sensitivity to preservatives, etc.

Tear substitutes[5]

Note:

- There is no evidence showing one product to be better than any other.
- Beware of development of preservative sensitivity in prolonged or frequent use (>4-6 x daily) - use preservative-free preparations. Also take into account preservatives in other eye medications, if used.
- Contact lenses:
  - Advise patients to discontinue contact lens wear during treatment. If this is impossible, use preservative-free drops and follow the manufacturer's instructions - eg, allow 30 minutes after application before putting in a contact lens.
  - Ointments should **not** be used with contact lenses.
- Caution if using other eye medication - tear substitutes may need to be instilled separately from other eye drops (see product leaflet).
- Most preparations (except acetylcysteine) are also available over the counter.

Drops

- Application - usually 3-4 times daily but can be used up to hourly as required.
- Various preparations - see the British National Formulary (BNF) under 'Further reading & references', below. Examples:
  - Hypromellose (needs frequent application).
  - Sodium chloride (useful as comfort drops or with contact lenses).
  - Sodium hyaluronate.
  - Products containing carbomers or polyvinyl alcohol are longer-acting.
- If there are visible strands of mucus, consider acetylcysteine drops, applied 3-4 times daily. These help to dispel sticky mucus. (A prescription is required and they may sting briefly.)

Gels

- Application: 3-4 times a day. They cling to the surface of the eye and hence need less frequent applications than drops.
- Examples: a variety of carbomers - eg, Viscotears®, GelTears®, Luiquivisc®.

Ointments

- Reduce evaporation of tears by coating the cornea.
- Best applied at night, as they can cause blurred vision due to the coating effect on the cornea. Contact lens wear is contra-indicated. Particularly useful in more severe cases of dry eye and in cases of recurrent corneal erosions.
- Examples - liquid paraffin, yellow soft paraffin.

Preservative-free preparations
Products available without preservatives include hypromellose, carbomers, polyvinyl alcohol, sodium chloride, carmellose sodium, hydroxyethylcellulose, and sodium hyaluronate. These are for those with severe symptoms, those who use soft contact lenses, those needing application more than six times per day, or those who develop irritation from the artificial tear products. The preservative most likely to cause eye irritation is benzalkonium chloride.

Further management - moderate or severe disease[4]

If things do not settle, advise use of preservative-free tear substitutes and refer for further management, which includes:

- Increasing dietary omega-3 fatty acids (oily fish or supplements). There is evidence that this reduces the risk of dry eye, but more studies are needed on optimal doses and exact preparations of supplements[6] .
- Anti-inflammatory agents - these may be more effective than tear substitutes:
    - Topical ciclosporin A - useful, as there are no systemic effects with topical use.
    - Topical steroids - long-term use is limited by side-effects.
    - Oral tetracyclines - have both antibacterial and anti-inflammatory effects. Where these are not tolerated, clarithromycin or azithromycin may be used.
    - Pilocarpine - for some with Sjögren's syndrome.

- Ocular insert:
    - Slow-release rods of lubricant inserted into the conjunctival sac - but may cause discomfort.
- Punctal plugs:
    - Temporary or permanent occlusion of lacrimal ducts to reduce tear drainage (various methods available).
    - There is some evidence to show this provides symptomatic relief in severe cases [7] .
    - Inflammation should be controlled first.
- Moisture retention:
    - 'Bandage' contact lenses - protect and hydrate the cornea.
    - Scleral lenses - create a tear-filled reservoir.
    - Moisture-retaining goggles.
- Secretagogues:
    - Pilocarpine can improve symptoms but side-effects can be problematic.
- Autologous serum tears:
    - Serum contains various nutritive and anti-inflammatory agents and no preservatives. The serum can be frozen and stored for use as eye drops.
    - There is currently no convincing evidence that autologous serum tears are more effective than traditional artificial tears [8] .

- Surgery:
    - Punctal closure with cautery and tarsorrhaphy.
    - Conjunctival surgery - eg, conjunctival graft or transplant, amniotic membrane transplant, salivary gland autotransplantation.

Complications

- Dry eyes are more susceptible to conjunctivitis.
- If severe, dry eye can lead to keratitis, corneal ulceration and infection, and corneal perforation (rare).

Prognosis

There is little formal research into the natural history of the condition, but it tends to follow a protracted course. The prognosis depends on the underlying cause if there is one. Loss of vision and corneal ulcers are rare.

Further reading

- Jackson WB; Management of dysfunctional tear syndrome: a Canadian consensus. Can J Ophthalmol. 2009 Aug;44(4):385-94.
- Dry Eye Syndrome - Preferred Practice Pattern; American Academy of Ophthalmologists, Oct 2013
- Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears; NICE Technology Appraisal Guidance, December 2015
- Messmer EM; The pathophysiology, diagnosis, and treatment of dry eye disease. Dtsch Arztebl Int. 2015 Jan 30;112(5):71-81; quiz 82. doi: 10.3238/arztebl.2015.0071.

Authored by:	Peer Reviewed by: Dr Colin Tidy, MRCGP	
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