

# Symptoms and diagnosis of dry eyes

Bo Hedqvist

Ögonspeglar AB, Järnhälsan, Göteborg, Sweden

## Symptoms

In most cases with Sjögren's syndrome (SS), dry eyes are the first, the most common and the most painful symptom of the disease. The symptoms of dry eyes are not specific for SS though, since many pathologic conditions can cause dry eyes. It is important to know that patients rarely use the word "dry", when describing their eye symptoms, but rather more often other expressions like burning, foreign body sensation or grittiness, itching, eye fatigue and blurred vision.

The precorneal tear film is composed of three layers: (1)

Covering the rough epithelial surface is a thin layer of *mucus*, which is closely bound to the epithelial cell membranes. The presence of a normal mucus layer is important for the stability of the tear film. The mucus is mainly produced by the conjunctival goblet cells.

The *tear fluid* makes up the bulk of the tear film. It is produced by the major tear glands and by the conjunctival accessory tear glands.

Covering the tear fluid is a very thin layer of *lipids*, produced by the meibomian glands of the eye lid margins. The presence of these lipids is important for the stability of the tear film and reduces evaporation of fluid.

There are two major causes of dry eyes: Reduction of tear fluid secretion and increased evaporation of tear fluid. Dry eyes in SS - keratoconjunctivitis sicca (KCS) - is one of the most common manifestations of decreased tear fluid secretion.

At the beginning of the disease, the symptoms often develop gradually over a period of months, but some patients experience a rather sudden onset. After this, the symptoms can be stable for several years. In everyday life, however, the severity of symptoms often varies from day to day and typically worsens during the course of the day.

Many patients report that the eyes feel "watery" although there is no tear flow. This is explained by the fact that there is often a certain degree of chemosis which is often perceived by the patient as excessive tear fluid. In some cases, there is indeed an excessive tearing which makes it difficult for the patient to accept the concept of the eyes being dry. The reason for the tearing is that the tear film dysfunction causes an ocular irritation, which leads to a reflex tear secretion. The tear fluid thus produced does not adhere to the ocular surface to form a proper tear film, due to imbalance of the components of the tear film, probably mainly an insufficiency of mucus. The result is tear flow that often overflows the edge of the lid margins, as the tear drainage system through the canaliculi is inadequate in relation to the amount of fluid produced.

## Diagnostic considerations

There are no clinical signs or objective tests that are specific for KCS and consequently none for SS. It is therefore necessary to establish classification criteria.

In the international literature, there is agreement on the fact that secondary Sjögren's syndrome (sSS) is present when the patient has another well-defined autoimmune disease together with KCS and/or dry mouth (stomatitis sicca) (2). It is therefore important that the diagnosis of KCS is correctly performed.

The question about which subjective symptoms and objective tests that shall be required to accept the diagnosis KCS and stomatitis sicca, has been extensively discussed. There is a tendency towards deciding on the diagnosis primary Sjögren's syndrome (pSS) in the presence of either KCS or stomatitis sicca. From the Scandinavian point of view, however, there is an agreement that pSS shall be diagnosed only if both KCS and stomatitis sicca can be demonstrated. We also feel that the

diagnosis of KCS and/or stomatitis sicca should be based on pathologic objective tests only. (Manthorpe, pers. comm.). Obviously, there are patients with symptoms, sometimes severe, but some patients with pSS that have remarkably mild symptoms especially young people and children. By eliminating subjective symptoms from the diagnostic requirements, we also avoid the situation where simulation of symptoms might affect the diagnosis.

Patients with KCS often have rather noticeably small, red eyes. Often there are crusts in the ciliae, signs of meibomitis and an increased amount of debris in the tear film. In severe cases, this can be seen without any instrument. The deficiency of tear fluid and the reduced amount of light reflectivity combined with the irregular blinking pattern give the observer the distinct impression of very painful eyes.

During the slit-lamp examination, these findings are confirmed and more subtle signs can be observed. Mucus strands adhering to the corneal surface as filaments (keratitis filiformis) is consistent with severe KCS.

### **Diagnostic tests**

*Break-up time (BUT)* is the measurement of the ability of the precorneal tear film to maintain its integrity. The test is performed by installing 2.5  $\mu\text{L}$  1% fluorescein solution in the conjunctival sac. Only pure fluorescein solution shall be used for this test, not any commercially available mixtures of fluorescein and anaesthetics. Of course, neither topical anaesthesia nor any other eye-drop that can affect the tear film shall be installed prior to the test. If a micropipette is not available, it is acceptable to use commercially available fluorescein paper strips, at least in everyday clinic practice. The paper strip should be moistened with isotonic saline prior to use. After a few blinks, the patient is asked to look straight ahead with eyes opened in a normal fashion. The tear film is observed in red-free light through the slit-lamp and the time from opening of the lids until the first dry spot appears, is recorded. The cut-off value is 10 seconds (3).

*The Schirmer-1 test (SIT)* was introduced by Schirmer in 1903. A standardised strip of filtering paper is applied over the margin of the lower lid. After 5 minutes with eyes lightly closed, the paper is removed and the length of the moistened part of the paper is measured. (4) In normal subjects there is a great variation, but patients with SS invariably display very low readings. The internationally accepted cut-off value is now 5 mm. (5) Previously, Schirmer's test was often performed with topical anaesthesia, which does not provide any further information. Performing SIT during stimulation of the nasal mucosa can sometimes be valuable, as this measures the maximal reflex tear secretion.

*Rose-bengal score dye test (RBS)* was used by Sjögren in his early work and the diagnostic value has been well established (6). 2.5  $\mu\text{L}$  1% rose-bengal is installed in the eye, and stains dying and desiccated epithelial cells without the protecting mucus layer. The amount of staining is expressed as a score, according to van Bijsterveld (4). One problem with this test is that the dye is rather toxic to the epithelium and the patients dislike it because of the intense stinging, burning sensation. As an alternative, lissamine-green can be used in the same concentration, as it stains in exactly the same pattern as rose-bengal. To alleviate the stinging effect of rose-bengal, it is advised to give the patient a topical anaesthetic after the test.

*The concentration of lysozyme and lactoferrin* in tear fluid is often significantly reduced in patients with SS. However, the tests are not widely used in clinical practice. Specificity and sensitivity is not very good.

*The osmolarity of the tear fluid* is increased in dry eyes, mainly because of increased evaporation in relation to secretion. The test can be made very accurately, but only with specialised and quite expensive equipment.

*Imprint-biopsy* is easily performed. It shows changes in the superficial cell layer of the conjunctiva. In patients with KCS, and especially SS, there is typically a condensation of the chromatin into snake-like figures.

*Biopsy of the lachrymal gland or the accessory tear glands* can demonstrate lymphocytic proliferation and acinar destruction. This test demands a high level of surgical expertise and it is not widely used.

In the Scandinavian countries, we use almost exclusively the “Copenhagen Criteria” for the diagnosis of KCS and SS. In my experience, this provides an excellent tool with a good, clinically significant specificity and sensitivity. In these criteria, KCS is present when at least 2 of the following tests are positive: BUT, S1T, RBS. pSS is present if there is KCS and stomatitis sicca. sSS is present when there is KCS and/or stomatitis sicca and a well-defined autoimmune disease, such as rheumatoid arthritis or SLE (2, 7).

## References

1. Bron AJ. Duke-Elder Lecture - Prospects for the dry eye. *Trans Ophthalmol Soc UK* 1985; 104: 801-26.
2. Manthorpe R, Andersen V, Jensen OA et al. Editorial comments to the four sets of criteria for Sjögren's syndrome. *Scand J Rheumatol Suppl.* 1986; 61: 31-5.
3. Lee JH, Kee CW. The significance of tear film break-up time in the diagnosis of dry eye syndrome. *Kor J Ophthalmol* 1988; 2: 69-71.
4. Bijsterveld OP. Diagnostic tests in the sicca syndrome. *Arch Ophthalmol* 1969; 82: 10-4.
5. Bjerrum KB. Tests and symptoms in keratoconjunctivitis sicca and their correlation. *Acta Ophthalmol Scand* 1996; 74: 436-41.
6. Prause JU, Kriegbaum NJ, Manthorpe R, Oxholm P. Rose bengal score. A possible key parameter when evaluating disease level and progression in primary Sjögren's syndrome. *J Autoimmun* 1989; 2(4): 501-7.
7. Manthorpe R, Oxholm P, Prause JU, Schiødt M. The Copenhagen criteria for Sjögren's syndrome. *Scand J Rheumatol Suppl.* 1986; 61: 19-21.