Oral and Ocular Manifestations in Sjögren's Syndrome

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ABSTRACT. ***Objective.*** Little is known about the relationship between lachrymal and salivary gland involvement in Sjögren's syndrome (SS). It is also of interest to know which eye test contributes most to the diagnosis of SS. We investigated the performance of different tear tests and how these tests relate to common serologic and salivary tests in SS.

Methods. In patients suspected of SS, the tear breakup time and the tear mucus score were evaluated in addition to the routine tests. Eighty consecutive patients were included, categorized into primary SS (pSS), secondary SS (sSS), and negative for SS.

Results. The tear breakup time and mucus score both performed insufficiently in diagnosing SS, in contrast to the Rose Bengal score. In pSS and sSS patients, a clear correlation was noted between tear and saliva quality and secretion rate, and between the Rose Bengal score and parotid sialography. Increased Rose Bengal scores also correlated significantly with hyperglobulinemia and presence of SSB antibodies in serum, with duration of subjective eye dryness, and with decreased tear gland function.

Conclusion. The Rose Bengal score remains the eye test of choice having the highest specificity for SS. Hyperglobulinemia and especially positive SSB serology may warrant close monitoring of the eyes, since these serum findings appear to relate to the severity of ocular surface damage. Theoretically, a positive evaluation of either the ocular or oral component, in addition to positive serology or histopathology, could be sufficient to diagnose the syndrome for clinical purposes. (J Rheumatol 2002;29:924–30)

Key Indexing Terms:
SJÖGREN'S SYNDROME OCULAR
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Sjögren's syndrome (SS) is considered a systemic autoimmune disease with the exocrine glands as main target organs. Since the tear and salivary glands are almost invariably affected, the oral and ocular sicca components form a significant part of this syndrome. The diagnosis of SS is based largely upon subjective and objective findings confirming damage or dysfunction of tear and salivary glands in accord with one of the international sets of diagnostic criteria[1].

Very little is known, however, about the differential involvement of the eyes and the mouth in SS. Further, it is of interest which eye test contributes the most to the diagnosis of SS. We investigated the performance of different eye tests, and determined how they relate to serologic and salivary tests used for diagnosing SS[2-5]. The eye tests studied were the tear breakup time, tear lactoferrin level, and a possible new test, the mucus score, in addition to the routine diagnostic tests, i.e., the Schirmer test and Rose Bengal score.

MATERIALS AND METHODS

Patients. Eighty consecutive patients were included in this study. All patients attended the outpatient clinics of the Department of Oral and Maxillofacial Surgery and the Department of Ophthalmology of University Hospital Groningen in the period August 1997 through April 2000, patients suspected of having SS were referred to both departments by rheumatologists, internists, neurologists, ear-nose-throat specialists, general practitioners, and dentists. Reasons for referral were not limited to ocular or oral manifestations such as eye dryness, mouth dryness, and swelling of the salivary glands, but also included arthralgia and fatigue. Diagnostic investigations for SS in all patients included: subjective complaints of oral and ocular dryness (Table 1), sialometry and sialochemistry, sialography, histopathology of salivary gland tissue, serology (SSA and SSB antibodies), and eye tests (Rose Bengal score, Schirmer tear test). As a reference standard for diagnosis of SS, the revised European classification criteria were used, categorizing cases as primary (pSS) and secondary SS (sSS) and as negative for SS (non-SS)[2-5]. The use of xerogenic drugs, i.e., antihypertensives, beta blockers, antihistamines, and psychotropics, was relatively frequent in all patients (in pSS 50%, sSS 56%, non-SS 69%).

Main outcome measures. As part of the investigation for eye dryness, tear

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Table 1. Ocular and oral symptoms according to the European criteria for the classification of SS[4].

Ocular symptoms (definition: a positive response for at least one of the following 3 questions)
1. Have you had daily, persistent, troublesome dry eyes for more than 3 months?
2. Do you have a recurrent sensation of sand and gravel in the eyes?
3. Do you use tear substitutes more than 3 times a day?
Oral symptoms (definition: a positive response to at least one of the following 3 questions)
1. Have you had daily feeling of dry mouth for more than 3 months?
2. Have you had persistently swollen salivary glands as an adult?
3. Do you frequently drink liquids to aid in swallowing dry food?

breakup time, tear fluid lactoferrin level, and a possible new test, the tear mucus score, were also measured for evaluation. Further, the duration of oral and ocular symptoms was recorded, defined as the time between referral and first complaints induced by or related to oral and ocular dryness, respectively. In addition to assessment of autoantibodies, serum immunoglobulin levels were measured.

Tear tests. The Schirmer test was carried out with a filter-paper strip (Whatman no. 41; 0.5 × 30 mm). The strip is placed in the lower fornix between the medial and lateral third of the eyelid of the unanesthetized eye. After 5 min, the amount of wetting is measured from the extrafornical position of the strip. A value ≤ 5 mm per 5 min was considered diagnostic for SS, according to the European classification criteria[3,6].

The Rose Bengal score, a quantified version of the original Rose Bengal test, was used to quantify the degree of staining. The test was performed by placing 1% Rose Bengal solution in the inferior fornix of both eyes and asking the patient to make one or 2 full blinks. The intensity of staining of both medial and lateral bulbar conjunctiva and of the cornea was scored, each section up to 3 points (1 = sparsely scattered, 2 = densely scattered, 3 = confluent) to a maximum score of 9[3,7,8]. A score ≥ 4 was considered diagnostic for SS according to the European classification criteria.

The tear breakup time is defined as the interval between a complete blink and the appearance of the first randomly distributed dry spots. A 1% fluorescein solution is instilled in the inferior fornix of both eyes. The patient is asked to blink a few times, and the interval in seconds between the last blink and the first break in the tear film is measured[3,7].

The tear fluid lactoferrin level was measured using a lactoplate kit (JDC, Culemborg, The Netherlands). A paper disc was placed in the lateral part of the inferior fornix of each eye and removed when completely damp (usually within 5 min). Each disc was then transferred to its corresponding reagent gel in the lactoplate kit and left for 3 days at room temperature. The diameter of the precipitate ring was measured and the lactoferrin concentration calculated using the table provided in the kit[3,9].

The tear mucus score was measured by semiquantitative clinical assessment. After evaluation of the Rose Bengal score, the debris in the cul-de-sac, which was then stained with Rose Bengal, was considered a clinical indication for mucus content. A scale from 0 to 3 was used, whereby 0 means no stained mucus at all in the cul-de-sac or on the cornea, 1 means mucus pellets in the cul-de-sac, 2 means mucus flocks in the cul-de-sac or the cornea, and 3 means mucus flocks as well as mucus threads in the cul-de-sac and on the cornea. This scoring was carried out every time by 2 observers and the mean value was noted.

Salivary tests. The methods of saliva collection and analysis (sialometry and sialochemistry) and the sialographic procedure were as described[10,11]. Glandular salivas were collected in a standardized manner. In brief, patients were instructed not to eat, drink, or smoke for 90 min preceding the sialometric assessment. All assessments were performed at a fixed time of day, in this study between 1:00 and 3:00 PM, to minimize fluctuations related to a circadian rhythm of salivary secretion and composition. All assessments were performed by the same observer. Glandular salivas were collected in preweighed plastic tubes from both individual parotid glands by using modified Lashley cups (Carlson-Crittenden cups), and simultaneously from the submandibular/sublingual (SM/SL) glands by syringe aspiration. Saliva from the SM/SL glands was collectively aspirated, as separate aspiration is rather difficult in clinical practice due to the close anatomical relationship between the orifices of both glands and the frequent presence of communicating ducts between the SM and SL main ducts.

Unstimulated salivary secretions were collected during 5 min, followed by collection of stimulated secretions during 10 min. The salivary glands were stimulated with citric acid solution (2% wt/vol) applied with a cotton swab to the lateral borders of the tongue at 30 s intervals. Mixing of the acid solution applied to the tongue and SM/SL saliva pooling anteriorly in the floor of the mouth (orifices of the SM/SL glands) was carefully avoided. The lag phase, defined as the time from first acid application on the tongue until first visible saliva secretion (in the tubes connected to the cups) was recorded for both parotid glands.

Whole salivary flow rate was determined by the draining method. Saliva is allowed to drip off the lower lip into a preweighed tube. At the end of a collection period of 15 min the patient expectorates into the tube.

After weighing the saliva samples to calculate flow rates (assuming specific gravity of saliva is 1.0 g/cm^3), sialochemical analysis was performed with the glandular saliva samples to quantify sodium, chloride, calcium, and phosphate. Sodium ions were measured by the flame photometric method with lithium ions as standard (3000 ppm). Chloride ions were measured by titration with silver ions. Inorganic phosphate was measured at 340 and 383 nm after addition of molybdate and reduction with bisulfite in the presence of p-methylaminephenolsulfate[12,13].

Statistical analysis. Data were submitted for statistical analysis using MedCalc version 5.0 to calculate receiver-operating characteristic (ROC) curves[14] and the Statistical Package for the Social Sciences (SPSS), version 9.0, for the remaining statistical procedures. These included independent sample t test and Spearman's correlation test. A significance level of 0.05 was predefined in all cases. ROC curves express the diagnostic accuracy of a test variable, by plotting the sensitivity of the test against the specificity at all possible thresholds. A flat curve indicates poor accuracy, whereas a curve that approaches the left corner of the diagram indicates high accuracy.

RESULTS

Study group. Using the European classification criteria for SS, 32 patients were classified as pSS (male/female ratio 2/30; mean age 53 yrs, SD 14, range 24–84), 25 patients as sSS (male/female ratio 6/19; mean age 58 yrs, SD 13, range 27–78), and 23 patients as negative for SS (male/female ratio 2/21; mean age 48 yrs, SD 12, range 20–70) (Table 2).

Diagnostic performance of tear tests. The tear breakup time performed poorly as a diagnostic test for SS, with a specificity of only 4%, when the original threshold of 10 s was used. ROC plot analysis revealed an optimum threshold at 3 s (≤ 3 s), with a sensitivity of 76% and specificity of 74% for SS (likelihood ratio 2.9) (Figure 1).

The tear mucus score had a sensitivity of 60% and specificity of 74% (likelihood ratio 2.3) when scores > 1.8 (on a scale of 0–3) were considered diagnostic for SS (Figure 1). If a threshold > 2.0 was applied the test gained specificity, at the cost of a serious loss of sensitivity, however (sensitivity 22%, specificity 95%, likelihood ratio 4.2). ROC plot analysis further showed that the diagnostic performance of

Table 2. Group characteristics. Data in parentheses are percentages.

	pSS, n = 32	sSS, n = 25	Non-SS, n = 23
Age (mean) at referral, yrs	53	58	48
Sex, (male/female)	2/30	6/19	2/21
Positive salivary gland biopsy	30 (94)	24 (96)	0 (0)
Positive serology	24 (75)	11(46)	3 (13)
SSA	24 (75)	11 (46)	2 (9)
SSB	13 (41)	8 (13)	1 (4)
Positive eye test(s)*	22 (71)	24 (96)	11 (48)
Schirmer tear test (≤ 5 mm/min)	16 (50)	17 (64)	10 (43)
Rose Bengal score (≥ 4)	19 (63)	19 (79)	6 (26)
Positive oral test(s)*	31 (97)	23 (92)	14 (61)
Parotid sialography**	28 (100)	16 (76)	3 (8)
Sialometry (UFWS ≤ 1.5 ml/15 min)	23 (72)	19 (83)	13 (57)
Subjective complaints *			
Dry eyes	27 (84)	23 (92)	17 (74)
Dry mouth	28 (87)	23 (92)	18 (78)

* According to European classification criteria: at least one positive eye/oral test, for subjective complaints see Table 1.
** Sialectasia present, percentages based on the number of patients with available information. UFWS: unstimulated flow of whole saliva.

the tear breakup time and mucus score are superior to the performance of the Schirmer test, with more rounded curves toward the upper left corner and larger areas under the curve. However, none of the tear tests could compare to the diagnostic value of the Rose Bengal score (Figure 1). It must be noted, however, that the estimates of diagnostic value of the Rose Bengal score and the Schirmer test are unavoidably somewhat flattered by an incorporation bias, for both tests were also used to support the diagnosis of the patients.

The diagnostic performance of the tear lactoferrin concentration test and its relation to other tests could not be properly determined due to a low sample size: only 22 patients had been tested when the manufacturer unpredictably withdrew the diagnostic kit for lactoferrin from the market.

Subjective manifestation: onset and duration. A 3 to 4 year diagnostic delay was observed in the SS patients studied, as estimated by the duration of their subjective complaints prior to diagnosis.

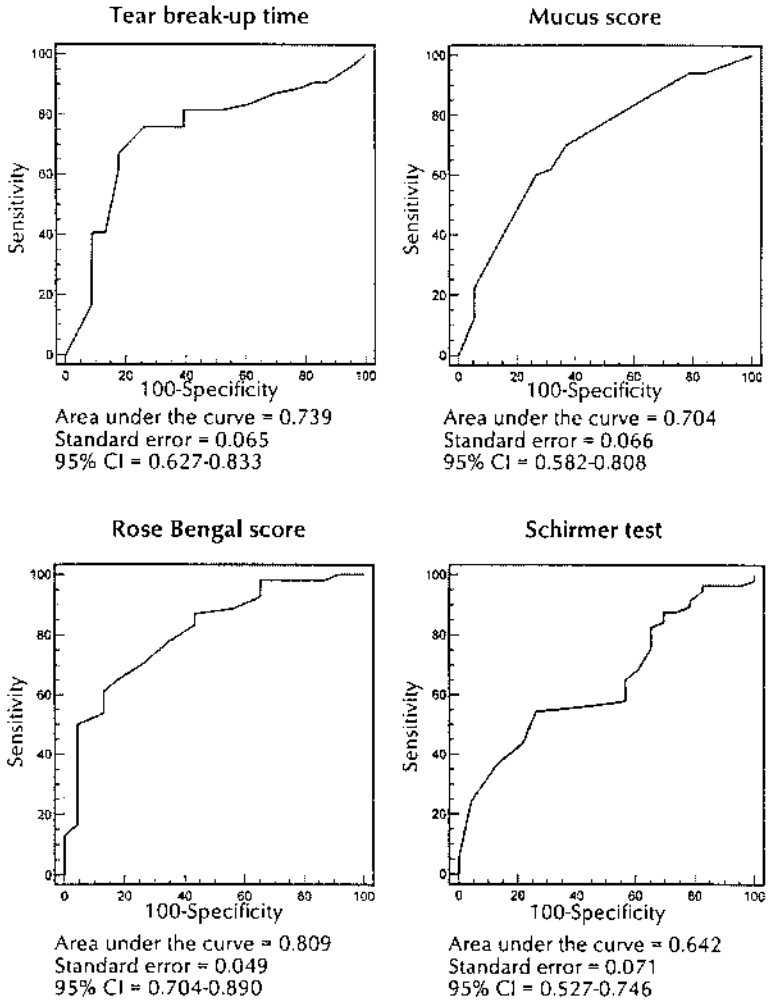

Figure 1. Nonparametric ROC curves of tear tests evaluated for use in identifying SS; 58 patients had SS, 23 did not. Note the relatively rounded curve, toward the upper left corner of the graph, of the Rose Bengal test, indicating good diagnostic performance.

No preponderance of either oral or ocular manifestations was found at the onset of SS; one-fourth of the SS patients reported mouth dryness as the first complaint, another one-fourth reported eye dryness as the first complaint, whereas one-third reported simultaneous onset of both mouth and eye dryness (Table 3).

Ocular manifestations. Rose Bengal scores were significantly increased and tear breakup times were significantly decreased in pSS and sSS patients, compared to non-SS. Further, Schirmer values were significantly decreased and mucus scores significantly increased in sSS patients, compared to non-SS (Table 4). According to the European classification criteria, 71% of the primary SS and 96% of the secondary SS patients tested positive for the ocular component. Notably, 48% of the non-SS patients also tested positive for the ocular component (Table 2).

Oral manifestations. Stimulated secretory flow rates of the SM/SL glands were significantly decreased in both pSS and sSS patients compared to non-SS (Table 5). In addition, the inorganic composition of saliva in pSS and sSS patients differed significantly compared to non-SS, with increased sodium and chloride concentrations and decreased phosphate concentration in stimulated parotid saliva (Table 5).

According to the European classification criteria, 72% of the pSS and 83% of the sSS patients tested positive for the oral component when only the sialometric criterion was applied (unstimulated flow rate of whole saliva ≤ 1.5 ml/15 min); 57% of the non-SS also tested positive for this sialometric criterion (Table 2). When only the radiographic criterion was applied (presence of sialectasia on a sialogram), 100% of the pSS and 76% of sSS patients tested positive, whereas only 8% of the non-SS patients did.

Serologic manifestations. Serum SSA and/or SSB antibodies were present in 75% of the pSS and 46% of sSS patients, compared to 13% of non-SS patients (Table 2). In addition, increased serum levels of immunoglobulins were observed in pSS and sSS patients; significance was reached only in pSS patients (Table 6).

Correlation between manifestations of tear and salivary gland dysfunction in SS. The Schirmer test as a measure of tear gland secretion correlated significantly with the stimulated secretion of the SM/SL salivary glands in SS patients (Spearman r 0.29, $p < 0.01$). In addition, the tear mucus score correlated significantly with sodium concentration in stimulated parotid saliva (Spearman r 0.26, $p < 0.05$).

Table 3. Onset and duration of symptoms of eye and mouth dryness in patients with SS (primary, secondary, and total), and non-SS patients.

	pSS, n = 32	sSS, n = 25	SS, n = 57	Non-SS, n = 23
Onset of first complaints, %				
Eye dryness before mouth dryness	16	40	26	13
Eye dryness only	3	8	5	9
Mouth dryness before eye dryness	31	20	26	13
Mouth dryness only	6	8	7	13
Simultaneous onset	34	24	30	39
Neither eye nor mouth dryness	10	0	5	13
Duration at first visit				
Eye dryness, (months, median)	38	50	43	31
Mouth dryness, (months, median)	44	34	39	31

Table 4. Ocular tests (mean ± SD) of primary SS (pSS), secondary SS (sSS) and SS negative patients (non-SS).

	pSS, n = 32	sSS n = 25	Non-SS, n = 23
Schirmer value, mm/5 min	8.2 ± 8.2†	4.5 ± 4.7*	10.2 ± 8.8
Rose Bengal score	5.0 ± 2.4*	5.7 ± 2.1*	2.7 ± 2.0
Tear breakup time	3.4 ± 3.9*	2.7 ± 3.3 *	5.7 ± 3.6
Mucus score	1.6 ± 0.8†	2.0 ± 0.7*	1.2 ± 0.8

†Significant difference between pSS and sSS.
* Significant difference between SS and non-SS (pSS vs non-SS and sSS vs non SS).
Independent sample t tests.

Table 5. Oral tests: salivary flow rate and inorganic composition (mean ± SD) of pSS, sSS, and non-SS patients.

	pSS, n = 32	sSS, n = 25	Non-SS, n = 23
Unstimulated flow rates			
Parotid, ml/min/gland	0.02 ± 0.03	0.01 ± 0.03	0.03 ± 0.07
SM/SL, ml/min/SM/SL gland	0.07 ± 0.12	0.02 ± 0.03*	0.10 ± 0.11
Whole saliva	0.11 ± 0.18	0.05 ± 0.08*	0.16 ± 0.22
Lag phase (s)	218 ± 237*	144 ± 178	62 ± 137
Stimulated flow rates			
Parotid, ml/min/gland	0.13 ± 0.15	0.15 ± 0.19	0.19 ± 0.12
SM/SL, ml/min/SM/SL gland	0.25 ± 0.30*	0.24 ± 0.35*	0.42 ± 0.25
Whole saliva	0.25 ± 0.30*	0.55 ± 0.68	0.79 ± 0.44
Composition stimulated saliva			
Parotid sodium, mmol/l	19 ± 18*	18 ± 22*	3 ± 3
Parotid chloride, mmol/l	26 ± 15	33 ± 27*	19 ± 8
Parotid phosphate, mmol/l	4.9 ± 1.8*	4.1 ± 1.9*	6.5 ± 2.4

*Significant difference between SS and non-SS patients; independent sample t test.
SM/SL: submandibular/sublingual.

Table 6. Serum immunoglobulin levels (g/L, mean ± SD) of pSS, sSS and non-SS.

	pSS, n = 32	sSS, n = 25	Non-SS, n = 23
Ig-total	26.5 ± 9.5*	22.4 ± 6.5	19.0 ± 6.5
IgG	20.1 ± 7.5*	17.1 ± 5.5	14.1 ± 4.9
IgA	3.3 ± 1.8	3.6 ± 1.7	2.9 ± 1.3
IgM	3.1 ± 3.8	1.7 ± 0.8	2.0 ± 1.2

* Significant difference between SS and non-SS patients. Independent sample T test. No significant differences were observed between pSS and sSS patients.

Correlation between imaging of ocular and oral pathology in SS. The Rose Bengal score correlated highly significantly with the severity of radiographic changes observed with parotid sialography (iodine contrast imaging) (Spearman r 0.39, $p < 0.01$) when radiographic changes were graded by their size and shape as punctate, globular, cavitary, or destructive sialectasia[15].

Correlation between ocular and serologic manifestations in SS. The total level of immunoglobulins in serum of SS patients and the presence of SSB antibodies correlated positively with the Rose Bengal score (immunoglobulins: Spearman r 0.22, $p < 0.01$; SSB: t test, $p < 0.05$).

Progression of ocular manifestation in SS. The Rose Bengal score was the only ocular manifestation that worsened significantly with increasing duration of subjective eye dryness (Table 7).

DISCUSSION

In this study, tear and salivary gland function in SS were extensively investigated in order to compare exocrine disease manifestations regarding onset, severity, and progression. Patients with SS manifested decreased values for tear and saliva secretion, altered quality and composition of tear and saliva fluid, and marked pathosis with imaging techniques (ocular staining and parotid sialography) compared to non-SS patients. In addition, the majority of patients with SS had positive serology for SSA/B autoantibodies and high immunoglobulin levels in serum. From all tear tests studied, the Rose Bengal score remained the test of choice regarding diagnostic accuracy. In analysis of independent results from tear, saliva, and blood tests, remarkably clear coherence was found within the SS patient group.

The tear breakup time test performed insufficiently in diagnosing SS. Despite the use of improved thresholds by ROC-plot analysis, tear breakup time achieved only moderate specificity and sensitivity as a test for SS. The low potential of the tear breakup time for discriminating between SS and non-SS patients is in accord with results from Vitali and co-workers[3]. The new tear test we evaluated, the tear mucus score, also performed insufficiently in diagnosing SS. Although the mucus score correlated highly significantly with all other eye tests (Rose Bengal score, Schirmer test, tear breakup time), it had poor sensitivity for SS, which impaired its use as a single test for diagnosing SS. However, since the observation of elevated mucus scores appeared to be very specific for SS (score > 2: specificity 95%), and the test requires nothing but simply observing the tear mucus after staining with Rose Bengal, it seems worth including the mucus score into the routine inspection of dry eye. Concerning the diagnostic performance of the tear and salivary tests currently included in the European classification criteria, no unequivocal conclusions can be drawn from this study, because the same criteria were used in this study to support the diagnoses by which patients were categorized. Therefore, the sensitivity and specificity calculated from these tests are flattered by an incorporation bias. Nevertheless, it can be concluded that both the Schirmer criterion (wetting ≤ 5 mm/5 min) and the sialometric criterion (unstimulated flow rate of whole saliva ≤ 1.5 ml/15 min) as proposed in the European classification criteria seem to produce many false positive test results (about half of the non-SS patients in our study tested positive for these criteria). When further evidence from future studies supports that these secretory tests are indeed rather nonspecific for SS, the thresholds of these tests should be critically reconsidered, or the tests should be replaced by tests with better diagnostic performance in the international criteria for SS. We consider measurement of stimulated SM/SL flow an excellent alternative for the current salivary flow test (measurement of unstimulated whole saliva), since it proved to be a very specific diagnostic test for the oral component of SS[16].

Studies have reported sialographic alterations (punctate, globular, cavitary sialectasia) to be related to a decrease in salivary gland function[17-19] and to the duration of complaints of oral dryness[11]. Comparable to these observations, the Rose Bengal score correlated significantly to decreased tear gland function (Schirmer test), altered tear film quality (tear breakup time, mucus score) and to the duration of subjective complaints of eye dryness. Since both sialography and Rose Bengal staining appear to relate to time, that is, duration of subjective complaints, and to glandular function, these 2 diagnostic techniques may have valuable use for monitoring disease progression of SS.

Table 7. Correlation (all Spearman r) between tear function tests and their relation to duration of subjective eye dryness in SS patients. Note the significant correlation of Rose Bengal score with the duraton of eye dryness and with all other tear tests.

	Duration, r	Schirmer Test, r	Rose Bengal, r	Tear Breakup Time, r	Mucus Score, r
Duration	—				
Schirmer test	–0.03, NS	—			
Rose Bengal	0.24, $p < 0.05$	–0.60, $p < 0.01$	—		
Tear breakup time	–0.05, NS	–0.52, $p < 0.01$	–0.70, $p < 0.01$	—	
Mucus score	0.04, NS	–0.57, $p < 0.01$	0.71, $p < 0.01$	–0.66, $p < 0.01$	—

NS: not significant.

A significant relation between tear and saliva secretion was found in SS, expressed by correlating lachrymal and SM/SL gland secretion. This correspondence in secretory dysfunction may be related to the fact that the lachrymal and SM/SL glands share the same seromucous exocrine function; in contrast, the parotid gland is a serous exocrine gland. As well, a significant correlation was observed between tear and saliva quality, expressed by correlating tear mucus score and parotid sodium concentration. There is, however, no proper explanation for this correlation, other than that both tests relate to SS. In previous studies, SM/SL secretion and the parotid sodium concentration were proven to be the most powerful predictors for SS of various sialometric and sialochemical variables[16,19-22].

In addition to the correlations between disturbances in tear and saliva secretion and quality in SS, a clear correlation was also noted between the Rose Bengal score and observations with parotid sialography, which is in accord with data from literature[18]. The Rose Bengal test, disclosing ocular surface damage resulting from tear gland involvement in SS, correlated highly significantly to parotid sialography, disclosing ductal damage resulting from salivary gland involvement. The correlation between the Rose Bengal score and the severity of sialectasia on a sialogram does not necessarily reflect an etiological connection, but might be the logical result when both relate to duration and severity of exocrine malfunction.

The tear tests did not only correlate with salivary tests, but also to serologic tests: the presence of SSB autoantibodies in serum and/or hyperglobulinemia appeared to be connected to more severe ocular surface damage measured by Rose Bengal staining. This suggests that SS patients with these findings in serum might be at risk for developing profound ocular surface damage, and hence may require close monitoring by an ophthalmologist.

The significant correspondence between the oral and ocular component in SS is a striking finding, because this actually suggests that, theoretically, the evaluation of only one component, complemented by serological or histopathologic confirmation, could be sufficient to diagnose the syndrome for clinical purposes. This would subject patients to fewer diagnostic procedures and achieve a quicker diagnosis with less discomfort. An exception to this theoretical reduction of investigation arises from patients who have tested positively for one component and have subjective complaints that indicate involvement of the other component as well. In such cases, additional evaluation is still required to assess whether there is a need for preventive measures or (symptomatic) treatment.

Reducing the diagnostic testing to only one sicca component should be the subject of further studies, because it departs from the classical diagnostic triad of Bloch and Buchanan[23]. For research purposes, it is evidently preferable to perform full diagnostic testing on both components, yielding maximum external validity.

We conclude that the Rose Bengal score remains the tear test of choice for diagnosing Sjögren's syndrome. It was observed that tear tests correlate strikingly with salivary tests. Thus, theoretically, a positive evaluation of one component (either ocular or oral) complemented by serological or histopathologic confirmation might be sufficient to diagnose SS, since both components appear to be related. Further diagnostic testing could be based upon clinical indication only. We determined that SSB autoantibodies in serum and/or hyperglobulinemia may warrant close monitoring of the eyes, since these appear to relate to more severe ocular surface damage.

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