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Keratoconjunctivitis sicca in leprosy

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Summary Our studies indicate that the patient with leprosy is at risk for developing keratoconjunctivitis sicca. The cause of keratoconjunctivitis sicca in our patients suggests that the aqueous layer of the tear film may be decreased as a result of a decrease in secretion of tears from the accessory lacrimal gland of the conjunctiva although it could also be decreased due to a diseased afferent arc to the lacrimal gland or to a diseased lacrimal gland both resulting in decreased aqueous production. In addition the stability of the precorneal tear film is probably affected due to a decrease in corneal sensation and to lagophthalmos both of which result in decreased blinking, as well as failure of the lid to resurface the tears because of irregularity of the conjunctiva or cornea.

Our results suggest that patients with leprosy should be followed closely for keratoconjunctivitis sicca and that treatment directed towards this problem should be initiated early.

Introduction

Absence of the precorneal tear film is a potentially serious problem in ocular leprosy, and this combined with corneal exposure is a major cause of blindness in these patients. In an effort to identify the individual components of keratoconjunctivitis sicca which might lead to corneal damage, we have carried out complete ocular examinations on 73 consecutive patients with biopsy proven leprosy who were seen at the Hansen's Disease Clinic in the San Francisco Bay Area. In the study we found a significant number with a decrease in the precorneal tear film.

Leprosy commonly affects the eyes. Moreover, ffytche has stated that leprosy affects the eyes more frequently than any other systemic disease.[1] Estimates of ocular complications in leprosy vary from 6% to 93%[2,3] and of the 10–15 million who suffer from the disease[4] possibly 5% are blind.[5] The periocular structures including the skin as well as the anterior segment of the eye are most frequently involved in leprosy, but the greatest threats to vision arise from lagophthalmos, chronic iridocyclitis, and keratitis. In our studies we therefore directed much of our attention toward determining the severity and frequency of exposure keratitis and loss of the precorneal tear film. The various parameters we studied included: the Schirmer tear test, tear lysozyme, corneal sensation,

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inability to close the eyes and lesions which might affect mixing and resurfacing of the precorneal tear film.

Patients and methods

Ocular examinations were performed at the Hansen's Disease Clinic, Seton Medical Center, Daly City, California. This is the second largest regional Hansen's Disease Clinic in the United States with approximately 500 currently registered patients with biopsy confirmed leprosy. Patients were referred for ocular examination by 1 public health nurse. Some were referred for specific ocular conditions but many were newly diagnosed patients with no apparent ocular pathology. These patients were referred to establish baseline information on their ocular status. The eyes of 73 consecutive patients were examined in the following order: 1, ocular history; 2, visual acuity; 3, Schirmer tear test (without anaesthesia); 4, external examination—brow, lid, skin; 5, slit lamp examination; 6, corneal sensation; 7, tonometry (applanation); and 8, (dilated pupil) fundus examination.

The Schirmer tear test was performed under standard conditions without anaesthesia, using a 5×35 mm Wattman 41 filter paper (Cooper Vision Pharmaceuticals). The edge of the paper was bent and placed over the junction of the medial and lateral $\frac{1}{3}$ of the lower eyelid of each eye. The patient was allowed to blink as desired. The amount of wetting in millimeters was measured after 5-min duration.

Corneal sensation was measured with a Cochet-Bonnet esthesiometer as described by Cochet and Bonnet.[6] The technique utilized a 0·0113 sq mm nylon monofilament which was gently touched perpendicularly to the cornea until the filament bent. The length of the filament was gradually decreased until the patient was able to feel the filament touch the cornea or the patient blinked, either of which was considered as the threshold of corneal sensation. The procedure was repeated several times to ensure accuracy. Four peripheral quadrants of the cornea and the central cornea were all tested. A conversion table for any measurement made with the esthesiometer is supplied by the manufacturer and is listed in Table 1.

The external examination and slit lamp examination were performed by one of us (HBO) and the results recorded on computerized forms for analysis.

To determine tear lysozyme values, the proximal 5 mm tabs of the filter paper used for the Schirmer tear tests were collected and stored in individual sterile bottles at $-5°C$ until studied. The specimens were eluted in phosphate buffered saline (pH 6·2) for 1 hour after agitation with a vortex mixer. Four aliquots of the solution were made and added to a solution containing Bactolysozyme substrate® (Difco Lab.). The solution was mixed and after sitting for half an hour the amount of light transmission through the substrate was analysed by a Bausch and Lomb Spectronic 21® spectrophotometer. The transmission of light was measured in percent, and the degree of transmission was compared to controls made and run at the same time. Duplicate samples of the specimens were run. The end points of transmission were read as normal, slight decrease, marked decrease and absent, with normal having a maximum light transmission of 86%.

Twenty-five patients selected from the patient's families and friends and of about the same age were used for control studies. Exclusion criteria for these patients were the presence of ocular

Table 1. Esthesiometer values

Nylon length (mm)	60	50	40	30	20	10	5
Unit decrease of corneal sensation	0	1	2	3	4	5	5·5
Mean values of pressure (mg)	11	13	21	36	75	145	200

symptoms or disease or any other underlying systemic diseases. They were tested with the Schirmer tear test strips, tear lysozyme determination and corneal sensation.

All data were coded and entered on a standard proforma for computerization. Results were analysed using Fisher's exact test corrected for small sample sizes.

Results

Of the 73 patients with leprosy 67% were males and 33% were females. All patients lived close to the San Francisco Bay area, but most had emigrated from other countries such as Mexico (32%), Philippines (28%) and Southeast Asia (32%). The distribution of disease classification as determined by biopsy is listed in Table 2. Patients with multibacillary disease accounted for 77% of the sample. This is proportionally similar to the population registered at this clinic.

Leprosy patients had significantly lower Schirmer test results from controls. Low (≤ 5 mm) Schirmer results, being indicative of loss of precorneal tear film were more common ($p = 0{\cdot}002$, Fisher's exact test) among leprosy patients. Abnormally low Schirmer readings were evident in 6% of the controls. Considering this as a background rate, the excess rate of abnormal Schirmer tests is $21{\cdot}9\% \pm 10\%$ among patients with leprosy (see Table 3).

Corneal sensation was moderately or markedly diminished in 40·8% of the eyes of leprosy patients studied and 10% of the eyes on non-patients ($p = 0{\cdot}002$). Non-patients can be expected to represent the background of the decreased corneal sensation in the non-leprosy population. The excess risk of diminished corneal sensation among patients can then be calculated at $30{\cdot}8\% \pm 12{\cdot}1\%$ (see Table 4).

Table 2. Disease classification of patients seen

Lepromatous	55%
Borderline lepromatous	21%
Borderline	1%
Borderline tuberculoid	20%
Tuberculoid	3%

Table 3. Quantity of tear fluid as measured by Schirmer strip

Schirmer measurement	By eye	
	Leprosy patient (%)	Normal (%)
Abnormal		
< 5 mm	39 (27·9) ($p = 0{\cdot}002$)	3 (6·0)
Normal		
6–10 mm	40 (28·6)	15 (30·0)
> 11 mm	61 (43·6)	32 (64·0)
Total	140 (100·0)*	50 (100·0)

* Six of the 146 eyes are without results; 4 did not complete this test and 2 denied cooperation.

Excess risk among leprosy patients $= 21{\cdot}9\% \pm 10\%$.

Table 4. Corneal sensation as measured by the Cochet–Bonnet esthesiometer

Corneal sensation measurements	By eye	
	Leprosy patient (%)	Normal (%)
Normal (no area decreased)	54 (45·0)	29 (58·0)
Slightly low (1 or more areas decreased one unit)	37 (30·8)	16 (32·0)
Moderately low (1 area decreased 2 units)	30 (25·0)	3 (6·0)
	$p = 0{\cdot}002$	
Markedly low (2 areas decreased 2 units)	19 (15·8)	2 (4·0)
Total	120 (100·0)*†	50 (100·0)

* The first 20 eyes were tested by cotton wisp, an unquantifiable instrument. These have been removed from the analysis. The results from 6/146 eyes were not available due to lack of cooperation (2 eyes) and failure to complete the examination (4 eyes).

† Numbers add to greater than 120 because of inclusion in more than 1 group.

Excess risk of moderately or markedly low corneal sensation in leprosy patients 30·8% ± 12·1%.

Table 5. Abnormalities of tear film or surfacing pathology

	Leprosy: No. eyes positive/No. eyes examined
Lagophthalmos	12/146 (8%)
Interstitial/Avascular keratitis	12/146 (8%)
Superficial keratitis	8/146 (6%)
Pterygia*	12/146 (8%)
Conjunctival scarring*	18/146 (12%)

* Not caused by leprosy.

Tear lysozyme values for both leprosy patients and controls were the same being slightly decreased in 32% of patients and markedly decreased in 8%.

The external and slit-lamp abnormalities which were present and considered as possibly the cause of pre-corneal tear film abnormalities are recorded in Table 5.

Stratification of patients into multibacillary and paucibacillary groups resulted in no differences being found for the Schirmer tear test, tear lysozyme or corneal sensation studies. Similarly, the pathology seen on external examination and slit-lamp examination only reflected the overall prevalence of disease types.

We were unable to accurately determine the duration of leprosy in many patients; therefore, we did not attempt to correlate our findings with duration of disease although it was our impression that the longer leprosy was present the greater was the prevalence of pathology and of abnormalities of the precorneal tear film.

Discussion

An adequate precorneal tear film is necessary to maintain healthy corneal and conjunctival epithelium. Furthermore, even in normal eyes, the tear film is unstable and must be constantly renewed and remixed through blinking. In instances in which the tear film does not adequately cover the cornea and conjunctiva, the epithelium may break down which can lead to discomfort, keratinization, scarring, vascularization, infection and even perforation of the cornea with loss of vision.

Traditionally the tear film has been divided into its various components, which include the lipid layer which is derived from the meibomian glands; the aqueous layer which is derived from the accessory lacrimal glands and lacrimal gland; and the mucous layer which is derived primarily from the conjunctival goblet cells. Our study using the Schirmer tear test would indicate that in a significant number of patients the aqueous component of tears is reduced, as compared to both our control patients and those of von Bijsterveld who studied the Schirmer tear test in over 1000 normal eyes.[7]

The tear lysozyme has been found to be a component of the aqueous which is produced by the lacrimal gland but not a component of the accessory lacrimal gland of the conjunctiva.[8] Our results therefore, suggest that the reduced Schirmer tear test was a reflection of a decrease in function of the accessory lacrimal glands.

Inasmuch as our examination dealt with the measuring of the Schirmer tear test prior to examining the patient at the slit-lamp, the tear break-up time itself was not evaluated. The tear break-up time is thought to be a reflection of the mucous component of the precorneal tear film. The mucous component is decreased in many instances in which there is scarring of the conjunctiva such as occurs in trachoma. Of interest however, is the fact that 20% (29/146) of the eyes examined had evidence of trachoma.

Irregularity of the conjunctiva (e.g. trachomatous scarring, keratinization), failure for the lid to properly surface the cornea with each blink as might occur from lagophthalmos, ectropion, or entropion, as well as decreased rate of blinking due to loss of the afferent limb of the blinking reflex all may affect the pre-corneal tear film. The function of blinking in which the closure of the lids tends to mix and restabilize the tear film is thought to play a large role in the stability of the tear film. Facial nerve weakness in lagophthalmos which was noted in 8% of the patients eyes in our study was significant. We are unable to state if interstitial keratitis or superficial keratitis which was seen in 8% and 6% respectively of our patients caused irregularity of the corneal surface and affected the precorneal tear film.

The measurements for corneal sensation in our study showed a significant decrease as compared to normal, suggesting that these patients are probably less sensitive to stimuli which usually caused blinking. This may predispose the patient to exposure as a result of poor resurfacing and stabilization of the tear film.

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TEACHING MATERIALS AND SERVICES

Technical Guide for Smear Examination for Leprosy

The first edition in English (1983) is now virtually out of print and a second (reviewed) edition is due to be published by the end of 1987. This Guide has been translated into French, Thai, Arabic, Spanish, Turkish and Bengali. A translation into Portugese has been done and is being prepared for the press. Hausa and Indonesian are in hand, but not yet translated. Distribution seems to have been fairly wide; for instance in the Eastern Mediterranean alone, Dr Wahdan, Director of Disease Prevention and Control for the Regional Office of WHO, has recently written to say that nearly 2000 copies were distributed to Arab-speaking countries in the Region—and the sales from distributing agencies in London and Oxford have been impressive. Addresses and method of application for the various translations will be published in the next issue of this journal. Meanwhile enquiries to Secretary, TALMILEP, DAHW, Postfach 348, D-8700 Würzburg, West Germany.

Leprosy for medical practitioners and paramedical workers; Ciba-Geigy

This booklet by R H Thangaraj and S J Yawalkar, published in 1986 by Ciba-Geigy, Basle, is now virtually out of print in its first edition—and has already been revised. Copies are available free of charge from The Medical Department, Ciba-Geigy, CH-4002, Basle, Switzerland. This is a high-quality booklet of about 100 pages, profusely illustrated in colour; extremely comprehensive; probably the most up to date and readable source of information of its kind currently available. It is being translated into French. It has been adapted and re-written for lay reading and 'basic information' and this version will probably be ready in early 1988.

Chart for Bacteriological Index (BI) in leprosy

This chart, giving a diagrammatic representation of the findings at BI 1–6 on the scale devised by Dr D S Ridley, and widely accepted in most parts of the world for slit-skin smears in leprosy, has been distributed to most leprosy endemic countries and also reproduced in various booklets and other items of health-learning material. WHO in Delhi recently produced and distributed 42,000 copies in India alone and has a reserve of several thousand more for other South East Asia countries. It should be A4 size (double the size as it appears in *Lepr Rev* 1986; **57,** 82) and despite the added cost, is best printed on card rather than paper, then laminated and sealed in plastic.

Guidelines for Tuberculosis Control Programmes, OXFAM

This OXFAM Practical Guide, No. 4, produced by the OXFAM Health Unit and written by Dr Paul Shears, is a handbook of 59 pages, first published in 1985, dealing with essentially practical issues in tuberculosis control. There are 15 chapters and 7 appendices, covering virtually everything of importance for control programmes in developing countries. There is much of interest and relevance for those working in leprosy in the pages of this inexpensive publication (£1.50, plus postage, per copy). OXFAM Health Unit, 274 Banbury Road, Oxford OX2 7DZ, England.

Teaching materials, The Leprosy Mission, London

Twenty-seven items of health learning material are available from TLMI in London, with recommendations on suitability for various levels of health staff. The entire list has recently appeared in the *International Journal of Leprosy*, Volume **55,** Number 2, 1987 and is available on request from: Teaching and Learning Materials, The Leprosy Mission (International), 50 Portland Place, London W1N 3DG. Some items are free, others have a basic charge; surface mailing is free, but air mailing is charged.

Education for Primary Health Care, Manchester, UK

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