

Conjunctival Appearance in Corneal Xerophthalmia

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● We studied the appearance of the conjunctiva in 50 consecutive cases of vitamin A-responsive conjunctival xerosis (X1) and 162 consecutive cases of nutritional keratopathy (corneal xerosis [X2] and stromal loss [X3]). Conjunctival xerosis, most extensive at or shortly after the onset of frank corneal involvement, was present in 101 (95%) of 106 eyes of cases of X2 but in only 99 (64%) of 155 ulcerated/necrotic eyes (X3A and X3B). Forty-four percent of involved eyes were inflamed, the percentage increasing with the severity of corneal disease. In 20 patients with nutritional keratopathy, conjunctival xerosis was monocular; inflammation was more prevalent and corneal involvement more severe in the nonxerotic eyes. In patients with precipitous deterioration of vitamin A status, clinically recognizable alterations of the cornea sometimes developed before any changes appeared in the conjunctiva.

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It is widely believed that xerophthalmic corneal destruction occurs in clinically "white and quiet" eyes^{1,2} in which the conjunctiva is distinctly xerotic.^{3,4} Our observations indicate that this is frequently not the case: xerophthalmic ulceration and necrosis are commonly accompanied by inflammation; conjunctival injection may mask background xerosis; and in severe precipitous deterioration of vitamin A status, clinically recognizable alterations of the cornea can precede those of the conjunctiva.

SUBJECTS AND METHODS

Between June 1977 and September 1978, a total of 162 consecutive children were seen at the Cicendo Eye Hospital, Bandung, Indonesia, with gross nutritional keratopathy. In 53 of the cases, the severest lesion was corneal xerosis (X2); in 50, small eccentric ulcers (X3A); in 34, larger areas of focal necrosis (X3B); and in 25, complete corneal destruction of one or both eyes (X3B). The corneal changes in these cases have already been described.⁵ The

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serum level of holoretinol-binding protein was severely and uniformly depressed in all subjects, and the serum vitamin A level was inversely related to the degree of corneal involvement.^{6,7} In most instances, viable corneal tissue responded rapidly to vitamin A therapy.^{8,9} Fifty children with vitamin A-responsive conjunctival xerosis but without frank corneal involvement, who were studied at the same institution, are described for comparison. They were the subject of a previous report.¹⁰

The normal deviated (z) and Student's t test were used in the statistical analyses.

RESULTS

The 162 cases of X2 and X3 contained 296 eyes with frank active corneal involvement. Conjunctival injection, often severe, was present in 132 (44%). Injection was more prevalent in eyes with stromal loss (X3) than in those with isolated corneal xerosis (Table 1) ($P < .001$).

Conjunctival xerosis was recognized in 101 (95%) of the 106 eyes of cases with X2 in at least one eye, but in only 152 (70%) of 216 eyes of cases with X3

in at least one eye ($P < .001$). Among the latter cases, conjunctival xerosis was more prevalent in nonulcerated eyes (53/61; 87%) than in eyes with corneal ulceration or necrosis (99/155; 64%) ($P < .01$). Two eyes of patients with X3 are omitted from the analyses: one was destroyed by a previous episode of xerophthalmia, and the record of the other failed to note the presence or absence of conjunctival xerosis.

Conjunctival xerosis was just as extensive in nonulcerated eyes of patients with X3 as in eyes of cases of corneal xerosis. It was more extensive in both than it was in cases of isolated vitamin A-responsive conjunctival xerosis (Table 2).

In 20 of the 162 subjects with corneal involvement, conjunctival xerosis was present in one eye but not the other. The nonxerotic eye was far more likely to be injected, and its cornea more severely involved, than its xerotic mate (Table 3).

Clinically apparent involvement of the cornea sometimes preceded that of the conjunctiva, particularly when vitamin A status deteriorated rapidly. One such patient's course is detailed in the following section.

REPORT OF A CASE

A 2-year-old boy with severe generalized malnutrition had bilateral conjunctival xerosis and X2 and an inferior ulcer in the left eye. Because his parents refused to allow hospitalization, he received only a single dose of 200,000 IU of oil-miscible vitamin A. Despite the persistence of severely decreased levels of albumin (± 1.7 g/dL) and transferrin (± 25 mg/dL), both eyes healed within nine days, holoretinol-binding protein and vitamin A levels peaking during this interval at $12 \mu\text{g/mL}$ and 32

Table 1.—Prevalence of Conjunctival Injection in Eyes With Nutritional Keratopathy*

Severity of Corneal Involvement	No. of Eyes	No. (%) of Eyes With Conjunctival Injection
Xerosis	143	21 (15)
Ulcer(s)	72	52 (72)
Focal necrosis	44	34 (84)
Complete necrosis	37	25 (68)
Total	296	132 (44)

*Presence or absence of injection was unrecorded in two cases. Difference in prevalence of injection between eyes with and without stromal loss was $P < .001$.

Table 2.—Extent of Conjunctival Xerosis (X1) in Eyes of Xerophthalmic Patients

Patient Classification	Total No. of Eyes	Extent of X1, No. (%) of Eyes			
		None	Temporal	Temporal and Nasal	$\geq 180^\circ$
X1	100	5 (5)	37 (37)	51 (51)	7 (7)
Corneal xerosis (X2)	106	5 (5)	9 (8)	42 (40)	50 (47)
Nonulcerated fellow eyes of X3 cases*	61	8 (13)	11 (18)	17 (28)	25 (41)

*Omits eyes for which record failed to note the presence or absence of X1. Difference in extent of X1 among cases with and without corneal involvement was $P < .001$.

Table 3.—Asymmetry of Inflammation and Corneal Involvement in Patients With Conjunctival Xerosis in Only One Eye

Case	Conjunctival Injection*		Severity of Corneal Lesion†	
	Xerotic Eye	Nonxerotic Eye	Xerotic Eye	Nonxerotic Eye
1	Absent	Present	X2	X2
2	Present	Present	Staphylococci	X3B
3	Absent	Present	X2	X2
4	Absent	Present	...	X3A
5	Absent	Present	...	X3A
6	Present	Present	X2	X3A
7	Absent	Present	X2	X3A
8	Absent	Present	X2	X3A
9	Present	Absent	X3A	...
10	Absent	Present	X2	X3B
11	Absent	Present	X2	X3B
12	Absent	Present	X2	X3B
13	Present	Present	X3A	X3B
14	Absent	Present	...	X3B
15	Absent	Present	X2	X3B
16	Present	Present	X3A	X3B
17	Absent	Present	...	X3B
18	Absent	Present	X2	X3B
19	Absent	Present	X2	X3B
20	Absent	Present	X2	X3B

*Difference between xerotic and nonxerotic eyes was $P < .001$.

†Clinical grading of corneal lesion: X2, corneal xerosis; X3A, corneal ulcer; X3B, keratomalacia.

μg/dL, respectively. One week later, his general condition had deteriorated further, with his weight for height decreasing from 85% to 59% of standard. Punctate keratopathy had returned. When visited by the study team eight days later, his general nutritional status was even worse, with gross pitting edema of both legs. The conjunctiva of both eyes appeared noninjected and nonxerotic, but both corneas were xerotic and contained small inferior ulcers. Eyelid closure was weak but complete, blinking was normal, and Bell's phenomenon was intact. The serum level of holotransferrin-binding protein was 0 μg/mL.

COMMENT

Because they were unaccompanied by supportive data, previous suggestions that inflammation^{11,12} and sudden deterioration of vitamin A status^{13,14} may modify the clinical appearance of xerophthalmia have largely gone unheeded. As a result, some children with classic xerophthalmic corneal involvement have been denied vitamin A therapy,¹⁵ and the origin of their corneal changes has been ascribed to protein-energy malnutrition,¹⁶ measles,¹⁷ and other illnesses.

Serum vitamin A levels are lower in cases of corneal xerophthalmia than in cases of isolated vitamin A-responsive conjunctival xerosis.⁶ In the present study, conjunctival xerosis was more extensive in cases with corneal disease (X2, X3) than in those without corneal disease (X1). It would appear that clinically recognizable

xerosis of the conjunctiva first appears in the temporal quadrant,¹⁰ followed by the nasal, the inferior, and finally, the superior quadrants. Involvement of 180° or more of the conjunctiva suggests established or incipient corneal disease.

Serum vitamin A levels are lower in patients with severe corneal disease than in patients with milder corneal involvement.¹⁸ Yet conjunctival xerosis was just as prevalent and extensive in eyes of patients whose worst lesion was X2 as it was in nonulcerated eyes of patients with more severe xerophthalmia. This would suggest conjunctival xerosis is already maximal at, or shortly after, the onset of frank corneal involvement.

The situation is complicated by corneal ulceration, conjunctival inflammation, and precipitous deterioration of vitamin A status. The conjunctiva is more likely to be injected and less likely to be xerotic in ulcerated than in nonulcerated eyes of patients with corneal xerophthalmia. This appears to be due to local rather than systemic factors, with inflammation masking (or reversing) the xerotic process. Among patients with monocular conjunctival xerosis, the xerotic eye was far less likely to be inflamed than the nonxerotic eye, and its cornea was less severely affected. Once corneal ulceration and necrosis occur, conjunctival injection becomes the rule.

In a small number of cases, precipitous deterioration of vitamin A status resulted in clinically recognizable alterations of the cornea preceding those of the conjunctiva, thus reversing the usual sequence. This provides at least one mechanism by which nutritional keratopathy can appear in the absence of both conjunctival xerosis and inflammation.

In differentiating nutritional keratopathy from infectious or other forms of corneal destruction, the presence of conjunctival xerosis is far more helpful than its absence. Clinically significant vitamin A deficiency should be suspected whenever X2, X3A or X3B are encountered in an appropriate dietary, social, or medical setting, regardless of the appearance of the conjunctiva.

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