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Immunoglobulins in tears in trachoma patients

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SUMMARY Tear immunoglobulin concentrations have been measured in 100 healthy people and 62 patients in different stages of trachoma. In healthy people the average IgA level was 27·8 mg/100 ml. There was no significant difference in the IgA level in various age groups and between the sexes. IgG was detected in 92 samples, and it was less than 1 mg/100 ml. IgM in tears was detected in only one sample. IgD was not detected in any specimen. In trachoma cases, the mean IgA level was found to be significantly lower (22·0 mg/100 ml) than in healthy people. There was no significant difference in IgA level between different stages of trachoma. IgG, IgD, and IgM could not be detected in any sample from the trachoma cases.

The pathogenesis of trachoma, a localised chronic disease of the eye, is not yet properly understood. Silverstein (1973) suggested that immunoglobulins may play some role. The immune components of trachoma are suggested by the prolonged follicular hypertrophy seen clinically and the dense infiltration of the conjunctiva by lymphocytes, plasma cells, and macrophages. Since plasma cells produce immunoglobulin, the tear immunoglobulin concentration may be altered in trachoma (McClellan *et al.*, 1974).

The main objective of the present study was to find out whether the tear immunoglobulin level alters in trachoma patients.

Patients and methods

The study was carried out among 62 trachoma patients and 100 healthy people chosen consecutively from the Eye Outpatient Department of Irwin Hospital, New Delhi, during the period from February to August 1976. The latter group comprised persons who had no evidence of ocular or systemic disease and who had attended mainly for the purpose of refraction.

An earlier report by the present authors has already described the IgA level among healthy Indian people (Sen *et al.*, 1976). However, for the purpose of the present investigation it was considered advisable to examine a fresh group of healthy persons to serve as concurrent controls for the study of trachomatous patients. Human tear specimens were collected by the technique as described previously (Sen *et al.*, 1976). The details of the cases are given in Table 1.

The sex ratio in the 2 groups (normal and trachoma) was almost the same. As for age, there was a slight difference between the 2 groups but, on the whole, it was not of a magnitude to warrant age standardisation of results. The trachoma stages were determined by clinical examination with the help of slit-lamp biomicroscopy by one of us (D.K.S.). The diagnosis was made in accordance with MacCallan's classification (MacCallan, 1913) as modified by the standards of World Health Organisation (WHO, 1962). The samples were stored at –20°C until needed. IgA, IgG, IgD, and IgM were quantified by a single radial immunodiffusion method (Mancini *et al.*, 1965). Mono-

Table 1 *Age and sex distribution of normal and trachoma patients included in the study*

	Normal persons		*Trachoma patients*					
	No.	*%*	*I*	*II*	*III*	*IV*	*All stages*	
							No.	*%*
Males	55	55·0	9	5	10	5	29	46·8
Females	45	45·0	9	8	9	7	33	53·2
Age in years								
0	4	4·0	—	—	—	—	—	0·0
5	7	7·0	1	1	1	—	3	4·8
15	44	44·0	15	11	5	4	35	56·4
35	14	14·0	2	—	3	11	16	9·7
45+	31	31·0	—	1	10	7	18	29·0
Total	100	100·0	18	13	19	12	62	100·0

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specific goat antisera against heavy chain human IgA, IgG, IgD, and IgM and the respective reference standards except that of IgA were obtained from Meloy Laboratories, Virginia, USA. The reference standard of secretory IgA purified from human colostrum was used.

Results

NORMAL CONTROLS

IgA was found in all the samples, the average being 27·8 ± 15·3 mg/100 ml. Its level in females (mean 30·1 ± 16·4 mg/100 ml) was somewhat higher than in males (mean 25·8 ± 14·4 mg/100 ml), but the difference does not attain statistical significance ($0·10 < P < 0·20$). Statistical analysis was carried out to determine if there was any correlation between age and IgA level. It was found that $r = 0·12$, $P > 0·10$, suggesting that there is no statistically significant correlation between the two. IgG was detected only in 92 samples and the concentration was less than 1 mg/100 ml in every instance. IgM was not detected in any of the samples except one, in which case it was less than 1 mg/100 ml. IgD was not detected in any sample

TRACHOMA CASES

Here again IgA was found in all the samples, the average being 22·0 ± 12·1 mg/100 ml. The mean level in successive stages of trachoma was 23·4, 23·1, 19·7, and 22·3 mg/100 ml respectively. The IgA level in different stages of trachoma and in healthy subjects is shown in Table 2.

Before attempting a comparison between the healthy people and the trachoma patients it is essential to ensure its validity. Apart from the randomness of the 2 samples (obtained by including healthy people and patients consecutively) there appear to be two more prerequisites for such a comparison, namely (1) that the 2 groups are similar in such respects as age and sex, and (2) that the trachoma patients, comprising, as they do, cases at different stages of the disease, are not a heterogeneous group. As to the first of these, it may be noted that the 2 groups are almost similar except for some slight differences in the age distribution. However, as we have seen, age does not appear to have any relationship with IgA level, and the minor differences in age distribution can be safely ignored. As to the second point, it is useful to compare the IgA level among patients at different stages of the disease. For this purpose an analysis of variance was carried out and the results are given in Table 3.

Table 2 *IgA level in mg/100 ml in healthy subjects and trachoma patients*

	No. of cases	*Mean ± SD*
Normal control	*100*	*27·8 ± 15·3*
Trachoma cases		
Stage I	18	23·4 ± 11·0
Stage II	13	23·1 ± 13·2
Stage III	19	19·7 ± 12·6
Stage IV	12	22·3 ± 12·6
All stages	62	22·0 ± 12·1

Table 3 *Analysis of variance*

Source of variation	*DF*	*Total sum of squares*	*Mean sum of squares*
Between the trachoma stages	3	150	50·0
Within the trachoma stages	58	8,771	151·2
Total	61	8,921	—

Between ss < within ss, hence formal test of significance unnecessary

It is clear that patients in various stages of trachoma do not differ significantly from each other in so far as the IgA level is concerned. It is therefore in order to combine them for a comparison with the healthy group of persons. As stated earlier, the mean IgA level among 62 trachoma patients was 22·0 compared to 27·8 among the 100 normals. This difference is statistically significant ($P < 0·05$).

Discussion

Chandler *et al.* (1974) found that the concentration of IgA in tears remained remarkably constant despite the presence or absence of disease. Maythar and Zakay-Rones (1972) estimated the concentration of IgA and IgG in tears from normal individuals and trachoma patients and found no significant changes in the 2 groups. McClellan and others (1974) found IgA and IgG levels in children with trachoma to be lower than in normal persons and the difference was statistically significant. Bluestone *et al.* (1975) have reported that IgG is usually detectable but only occasionally quantifiable in tears from normal and diseased eyes. In our series we found lower IgA levels in cases with trachoma than in healthy persons and the difference was highly significant statistically. We also found IgG to be detectable, though not quantifiable, in 92 out of 100 healthy persons but undetectable in all trachoma cases.

It is difficult to understand why an infected group should have a lower immunoglobulin level. It has been postulated that the low level of immunoglobulin in tears from trachoma patients may be due to the inflammation in the upper fornix, which

partially occludes the opening of the lachrymal tubules and prevents stimulation of the lachrymal gland plasma cells or interferes with the flow of tears down the tubules (McClellan *et al.*, 1974). Another suggestion is that the immunoglobulin deficiency in persons suffering from trachoma is inherent, which makes them prone to infection by trachoma agents. We are inclined to think this is more plausible. It has been suggested that immunoglobulin in tears provides the body with a first line of defence against invasion by micro-organisms. South *et al.* (1968) showed that immunoglobulin-deficient children were subject to recurrent conjunctivitis. Kaufman (1969) has reported a superficial keratitis among patients with hypogammaglobulinaemia who had no demonstrable IgA in their tears.

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References

Bluestone, R., *et al.* (1975). *British Journal of Ophthalmology*, **59**, 279.

Chandler, J. W., *et al.* (1974). *Investigative Ophthalmology*, **13**, 151.

Kaufman, H. E. (1969). Development of resistance in the eyes. In *Conference on Secretory Immunoglobulins*, Beto Beach.

MacCallan, A. F. (1913). *Trachoma and its Complications in Egypt*, p. 5. London, Cambridge University Press.

McClellan, B. H., Bettman, J. W., Jr., and Allansmith, M. R. (1974). *American Journal of Ophthalmology*, **78**, 106.

Mancini, G., Carbonera, A., and Heremans, J. (1965). *Immunochemistry*, **2**, 235.

Maythar, B., and Zakay-Rones, Z. (1972). *Investigative Ophthalmology*, **11**, 651.

Sen, D. K., *et al.* (1976). *British Journal of Ophthalmology*, **60**, 302.

Silverstein, A. M. (1973). *Immunologic Modulation of Infectious Disease Pathogenesis*. Friedenwald Lecture. Read before the Association for Research in Vision and Ophthalmology Meeting, Sarsota, 6 May.

South, M. A., *et al.* (1968). *American Journal of Medicine*, **44**, 168.

World Health Organisation (1962). Expert Committee on Trachoma: Third Report. *World Health Organisation Technical Report Series*, No. 234, p. 9.

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Notes