THE WEIL-FELIX REACTION IN TRACHOMA

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Introduction

The lack of conclusive evidence that any of the bacteria which can be isolated from trachoma are causally related to the disease has led to a search for some other variety of infective agent, and in recent years considerable attention has been focused on the so-called Halberstaedter-Prowazek bodies which can be found in scrapings from the conjunctival epithelium of trachomatous patients. The nature of these bodies, and their relation to the disease, are at present somewhat uncertain, but many workers regard them as *Rickettsias*. Cuenod, Nataf & Loukitch (1938) claim that, like the *Rickettsia* of typhus, the Halberstaedter-Prowazek bodies can be cultivated in the intestine of the louse, and that they have produced trachoma in a monkey with material from inoculated lice after the third passage in the louse.

Pursuing the analogy between trachoma and typhus further, certain workers claim to have found that the Weil-Felix reaction, which is of diagnostic value in typhus, is positive also in a significant proportion of trachoma cases. Thus Derkač (1937) found positive reactions in five out of twenty sera from trachoma cases, and similar results were obtained in a larger series of cases by Pŏstič (1938). Poleff & Nain (1938) found that the Weil-Felix reaction was positive in a high proportion of trachoma patients in Morocco, especially during the active stages of the disease. In Belgrade, Djourichitch & Loukitch (1938) found that during the early stages of the disease the sera of trachoma patients more commonly agglutinated *B. proteus* OX19 than the sera of non-trachomatous controls, while in the later stages of the disease the positives were twice as common in the trachoma cases as in the controls. These authors, however, accepted as positives agglutinations in somewhat lower titres than those which are generally regarded as having any significance. Noury (1938), examining the sera of trachoma patients in Morocco, obtained twenty-one positive Weil-Felix reactions among forty sera with *Proteus* OXK, four positives in seventy sera with OXN, and no positives in seventeen sera with OX19; with a *Proteus*-like organism (TrN), isolated by blood culture from a case of trachoma, twenty-three out of fifty-one sera from trachoma patients produced agglutination in significant titres. In Tunis, on the other hand, Durand & Lumbroso (1938) found no significant difference in the mean titre at which complete agglutination occurred in fifty-six trachomatous sera and

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twenty non-trachomatous sera with emulsions of OX19, OXK, OXL, and TrN. Julianelle (1938) regarded as inconclusive certain tentative experiments with *Proteus* X19 and X2 which he commenced in 1934, but did not complete.

The evidence relating to a positive development of the Weil-Felix reaction in trachoma is therefore contradictory, and it is our opinion that none of the observations cited can be accepted as conclusive, owing to the fact that sufficient cognisance has not been taken of other conditions present locally which might account for the positive reactions, irrespective of trachoma. In some of these observations no controls are recorded; most of them have been carried out in localities where typhus and allied fevers are known to exist; in those instances where proper controls have been made, the proportion of positive reactions among the controls was appreciable, and in no instance was the series numerically large, so it is doubtful whether any significance can be attached to the differences observed between the incidence of positives in trachoma patients and in the controls.

Workers who are in favour of a Rickettsial origin of trachoma maintain that the demonstration of a positive Weil-Felix reaction provides strong evidence in support of their theory.

For reasons about to be discussed, conditions in the Sudan are particularly favourable for the investigation of this hypothesis.

Trachoma and typhus in the northern Sudan

Trachoma is prevalent in the northern Sudan. On the other hand, typhus fever has never been reported clinically in the Sudan, and in order to determine whether this absence of typhus is real or merely apparent a serological survey was carried out during 1937 on 1000 human sera from various parts of the country and 240 sera from wild rats (Horgan, 1938). With the exception of two doubtful tests, the results were entirely negative, and it is interesting to note that these negative results were obtained in spite of the fact that a certain proportion of the sera must have come from people suffering from trachoma.

Dr E. S. Horgan suggested to the present writers that this valuable record not only supported the clinical evidence with regard to the absence of typhus in the Sudan, but also indicated the Sudan as a particularly suitable field for the work recorded in the present paper, because the results of the Weil-Felix reaction in a representative section of the population were already known, and provided a clear cut negative control, against which the results in a series of trachomatous sera could be readily assessed.

Material

The sera tested in the present investigation were obtained from cases diagnosed clinically as trachoma in the Ophthalmic Department of Khartoum River Hospital. The patients were of Sudanese nationality, and the age distribution was as follows:

1– 9 years	12 cases
10–19	52
20–29	50
30–39	30
40–49	22
50 years and over	34
Total	200

Poleff & Nain (1938) found that the frequency of positive Weil-Felix reactions in trachoma is influenced by the stage of the disease. For this reason care was taken to ensure that sera from patients in all stages of the disease were included in the present series. Using MacCallan's (1936) classification of trachoma, the frequency distribution of the various clinical stages was:

Tr. i	12 cases
Tr. ii	14
Tr. iii	56
Tr. iv	118
Total	200

Quite 50% of the cases classified as Tr. iv presented a clinical condition which we designate locally as Tr. Q. By this we mean trachoma which has become entirely quiescent without the complete scarring described by McCallan as typical of the stage Tr. iv. Such cases have had trachoma at some previous time, but came to the "outpatients" on account of some other eye condition, e.g. cataract, glaucoma, etc.

METHODS

Three suspensions of *Proteus* were used, OX19, OX2, and OXK, of which OX19 and OX2 were alcoholized agar cultures but OXK was a formolized broth culture, because for some unknown reason all alcoholic suspensions of agar cultures of this strain showed some spontaneous agglutination. The strains were obtained originally from the National Collection of Type Cultures, London. Suspensions were made and standardized at 300 million organisms per c.c. according to the methods described by Gardiner (1931). The tests were incubated in a water bath at 52° C. for 4 hr., and left at room temperature for 24 hr. before being read.

In a series of thirty sera parallel tests were put up against living suspensions of the three strains, but as no significant differences were noted in the results, no further work was carried out with living suspensions.

RESULTS

None of the 200 sera produced agglutination in significant titres (1 : 50) with OX19 and OX2. With OXK agglutination in titres of 1 : 50 or more was produced by five sera. Of these the end point was 1 : 125 in one serum and 1 : 50 in the remaining four. It is doubtful if any significance can be attached

to the latter, since OXK suspensions, being more sensitive than those of OX2 and OX19, are commonly agglutinated to a higher end-point by normal and specific sera alike. The serum which agglutinated up to 1 : 125 was that of an old woman, aged about 80 years, and was taken originally for a Kahn reaction. The condition of her lids was that of Tr. Q, and had been so for many years; the trachoma was only discovered on routine clinical examination. Her serum was tested on two occasions, on both of which it agglutinated the OXK suspension up to the same titre (1 : 125).

In dilutions of less than 1 : 50 positive reactions were relatively more frequent among the 200 sera from trachoma patients than in the 1000 sera tested during the typhus survey, but in a further twenty-two sera from specially selected non-trachomatous individuals the results were comparable.

The results of the complete test in 222 sera may be conveniently summarized in tabular form, the positives in each group being expressed as percentages. Through the kindness of Dr E. S. Horgan, the figures of the 1937 typhus survey are included in the table for comparison.

Table I. *Results of the Weil-Felix reaction in* 200 *sera from cases of trachoma compared with the results on* 22 *sera from non-trachomatous persons and in* 1000 *sera taken in a typhus survey*

Serum dilutions	OXK			OX2			OX19		
	Typhus survey %	Trachoma cases %	Non-trachomatous controls %	Typhus survey %	Trachoma cases %	Non-trachomatous controls %	Typhus survey %	Trachoma cases %	Non-trachomatous controls %
1 : 12·5	9·8	14·5	18	0·4	1	0	0·3	1	0
1 : 25	0·5	14	29	0	2	0	0	0	0
1 : 50	0·1	2	9	0	0	0	0	0	0
1 : 125	0	0·5	0	0	0	0	0	0	0
1 : 250	0	0	0	0·1	0	0	0	0	0
1 : 500	0·1	0	0	0	0	0	0	0	0
Total no. of sera in each group	1000	200	22	1000	200	22	1000	200	22

Summary

1. Various workers in different countries claim that in the sera of trachoma patients a positive Weil-Felix reaction is found and regard this as evidence that the causal agent of trachoma is a *Rickettsia*.

2. The examination of 200 sera from trachoma patients in the Sudan has failed to reveal any significant differences with regard to the Weil-Felix reaction between them and twenty-two sera from non-trachomatous controls, or 1000 sera taken, without reference to trachoma, from a large and representative section of the population.

3. Clinical and serological evidence suggest that typhus is absent from the Sudan. For this reason the interpretation of results is less liable to confusion in the Sudan than in countries where positive Weil-Felix reactions may occur in a varying proportion of the population due to typhus infections.

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