Correspondence

TO THE EDITOR, *British Journal of Venereal Diseases*

Quantitative microhaemagglutination assay for *Treponema pallidum* antibodies in humans

Sir,

Tight and White[1] in their paper entitled "Quantitative microhaemagglutination assay for *Treponema pallidum* antibodies in experimental syphilis" discuss certain shortcomings of studies on the quantitative microhaemagglutination assay for *Treponema pallidum* antibodies (MHA-TP) in humans. These authors suggest that data on specific areas requiring further study, which include the effect of treatment on MHA-TP titres and the value of the MHA-TP as an indicator of reinfection, could be readily obtained by performing sequential quantitative non-treponemal and MHA-TP tests on follow-up sera. Such follow-up has been standard policy in Edinburgh for several years and some information relevant to Tight and White's suggestions has already been published.[2] We would like to summarise the main points.

The response of the MHA-TP to treatment was studied in 61 cases of early infectious syphilis. In none of the 55 cases of early syphilis in which the pre-treatment MHA-TP result was positive did the test give a consistently negative result after treatment. In primary and early latent syphilis it was not possible to demonstrate any significant changes, but in some cases of secondary syphilis a significant and rapid fall in MHA-TP titre occurred with treatment. In general the titre decreased significantly within four months of treatment for secondary syphilis to a level which was maintained more or less steady thereafter. This finding is at variance with the suggestion of O'Neill[3] that the post-treatment MHA-TP titre reflects the stage at which the disease was arrested, declining subsequently only slowly, if at all, with time.

Reinfection with secondary syphilis occurred in three cases; in each case there was a significant increase in MHA-TP titre and a parallel increase in the Venereal Disease Research Laboratory (VDRL) test titre. Because of the interval between follow-up tests it was impossible to say whether the increase in MHA-TP titre preceded that of the VDRL test or vice versa. Two of the reinfected patients had shown significant reductions in the MHA-TP titre after treatment of the original infection. After treatment of the reinfection the titres again fell, although more slowly, and in one a fall was not observed until 12 months after treatment.

Yours faithfully,

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TO THE EDITOR, *British Journal of Venereal Diseases*

Antenatal screening for syphilis

Sir,

The results of the *Treponema pallidum* haemagglutination (TPHA) test and the Venereal Disease Research Laboratory (VDRL) test were reviewed on sera from 7140 antenatal patients seen between 1976 and 1979. The fluorescent treponemal antibody-absorbed (FTA-ABS) test was used when confirmation was required (table). The serological methods have been described.[1 2]

The TPHA test gave a positive result for 53 (0·74%) sera, although the FTA-ABS test failed initially to confirm the TPHA reaction in 15 of those 53 sera in which it was the only test giving a positive result. On testing further samples, the positive TPHA results could not be reproduced in two patients and the FTA-ABS test result remained negative; in four patients a positive TPHA test result was found in association with a positive FTA-ABS reaction, while subsequent samples were not received from the remainder. Thus, 42 (0·59%) patients had definitely confirmed positive treponemal test results. If the TPHA test had not been used for screening, only 17 (0·24%) sera would have given a positive result, a figure comparable to that found by Hare[3] on sera from the antenatal patients attending the nearby Queen Charlotte's Hospital, London.

TABLE *Number of sera with positive test results*

Serological test results	*No*	*%*
TPHA+, FTA/ABS+, VDRL−	21	32·3
TPHA+, FTA/ABS−, VDRL−	16*	24·6
TPHA+, FTA/ABS+, VDRL+	12	18·5
TPHA+, FTA/ABS−, VDRL+	5	7·7
TPHA−, FTA/ABS+, VDRL+	0	
TPHA−, FTA/ABS+, VDRL−	0	
TPHA−, FTA/ABS−, VDRL+	11	16·9
Total	65	100

+ Positive − negative
*Includes one doubtful positive TPHA result at a serum dilution of 1/80.

Biological false-positive VDRL reactions were found in 11 (0·15%) sera. The patients whose sera were reactive in the VDRL test alone were not treated; they had normal deliveries at term, and in none of the offspring was there any evidence of congenital syphilis. Five patients in whom only the TPHA test gave a positive result likewise had normal deliveries and offspring. The remaining four such cases were untraceable.

Titres of the VDRL reaction and the TPHA test (from 80 upwards) tend to correspond[4] but both tests do not always give a positive result for the same serum from patients with primary syphilis. Lesinski and his colleagues[5] showed that in 57 patients with primary syphilis there were six (11%) whose sera gave a positive VDRL reaction but a negative TPHA test result. The TPHA test result may not only be positive when the VDRL test result is negative in primary syphilis,[5] but exceptionally the TPHA test result may

become positive before that of the FTA-ABS test.[6,7] The reason for the delayed reactivity of the TPHA test in a small number of cases of primary syphilis is not clear. It is not likely to be a lack of reactivity of the TPHA test to IgM antibody, as in early experimental treponemal orchitis the bulk of the TPHA antibody is found in the 19S fraction.[8]

The advantage of performing the VDRL test in addition to the TPHA test is certainly not manifest in this small series. If the VDRL test were omitted there would be a saving not only of the cost of the test, but the additional investigations during pregnancy and postpartum would have been avoided. Microscopical assessment required in the FTA-ABS test precludes its use for screening large numbers of sera in most routine laboratories.

The abandonment of the VDRL test as a screening test is supported by its failure to detect further cases of syphilis in this series of antenatal sera, provided that the TPHA test is used. Thus the TPHA test might become the sole screening test in antenatal serology as long as syphilis remains an uncommon disease.

We would like to thank Professor N Morris for access to his patients' case notes.

Yours faithfully,

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TO THE EDITOR, *British Journal of Venereal Diseases*

Attempted BCG immunotherapy for condylomata acuminata

Sir,

There is mounting evidence that cellular-mediated immunity (CMI) plays an important role in the resolution of human wart disease, although the exact mechanisms by which this occurs are not yet fully understood.[1-3] Various immunological treatments have been employed in the therapy of warts, including autogenous vaccine[4-6] and topical dinitrochlorobenzene,[7-9] with good results reported in most series of patients. Proponents of these measures believe that such therapy provokes a host immune response in patients with wart disease resulting in the immunological rejection of wart tissue. Following this line of reasoning, we proposed treating a group of patients with highly-resistant condylomata acuminata by BCG immunotherapy.

Six patients (five male and one female) were studied with biopsy-proven condylomata acuminata, whose mean duration was 8·4 years (range 2-35 years). In all patients previous forms of conventional therapy, which included repeated applications of topical podophyllin 25% in tincture of benzoin, had failed.

Patients were begun on a weekly series of vaccinations using University of Illinois BCG-Tice vaccine. An approximate concentration of 5×10^8 organisms per treatment were administered by the tine plate or scarification method or both. The mean number of treatments per patient was nine.

The sites chosen for vaccination varied somewhat from patient to patient but generally included the lower pubic and inner thigh areas adjacent to large clusters of lesions. Attempts were made to inject BCG intralesionally with a syringe but the villous nature of the lesions made this technically difficult. We were able to inject BCG successfully into the base of several lesions of two patients on three different occasions each, but both patients complained of such intense local pain that we were forced to abandon this approach in favour of the techniques described above.

Patients were followed closely for any change in the appearance of their lesions. While four out of five patients became sensitised to BCG, with development of pustules and local erythema at the tine and scarification sites, no significant changes (either quantitative or qualitative) were observed in their adjacent condylomata lesions. It was further observed that the injection of BCG at the base of the lesions in two patients highly sensitised to BCG on areas of normal skin completely failed to provoke an inflammatory response.

The lack of an equivalent inflammatory response to BCG injected into the immediate vicinity of the condylomata in BCG-sensitised patients at first seemed difficult to explain. A further search of the literature showed that a similar phenomenon was recently reported by Freed and Eyres, whose patient with recalcitrant hand warts responded positively to PPD injected into normal skin yet PPD injected intralesionally produced no inflammatory response.[10] It was subsequently shown by in-vitro methods that this patient's wart tissue contained a potent "blocking factor" capable of supressing a normal CMI response.

The presence of "blocking factor" could explain the observations of this study. Further characterisation of this substance, particularly its origin and mechanism of interaction with the immune system, may perhaps shed new light on our understanding of human tumour immunology.

Yours faithfully,

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