

ANNOTATION

THE TREPONEMAL IMMOBILIZATION TEST

Experimental work on the immune processes in syphilis has hitherto been hindered by the inability to cultivate the causative organism. Although several strains of treponemata have been grown in artificial media, it is generally considered that they are not virulent *T. pallidum*. Nelson (1948) used the testicles of rabbits suffering from an acute orchitis produced by the intra-testicular inoculation of the Nichols strain of treponemata as the source of organisms. He developed a medium in which *T. pallidum* will remain viable for periods up to 8 days. Definite evidence of multiplication has not been obtained. The Nichols strain is thought to have maintained its virulence because accidental infection of human subjects has occurred. When a suspension of treponemata in this medium is exposed to the action of a syphilitic serum in the presence of complement, immobilization of the organisms occurs; on the basis of this observation, Nelson and Mayer (1949) developed their "Treponemal Immobilization Test".

The immobilization appears to be due to a true antigen-antibody reaction which is dependent on the presence of complement. Animal experiments with the immobilized treponemes suggest that they are non-infectious and therefore presumably dead.

The results of examination of normal and syphilitic human sera by this test were reported by Nelson and others (1950). Negative results were obtained with the sera of eighty normal persons. The test was negative in 87 and "unsatisfactory" in three of ninety sera from patients with diseases other than syphilis, in whom there was no history of syphilis. Positive results were found in two-thirds of 53 primary cases, in all of 51 secondary, 50 latent, and 82 late cases of syphilis. Similar findings were reported by Magnuson and Thompson (1949); these workers, however, found the test negative in about half the cases of primary and in 14 per cent. of the cases of secondary syphilis.* Small numbers

of sera have been examined in France by Durel and others (1951), and Vaisman and Hamelin (1951). Among Nelson's cases it is noteworthy that there were seven patients with symptomatic late syphilis whose standard serum tests were all negative; immobilizing antibody was demonstrated in all of them. This antibody was also found in the cerebrospinal fluid of four out of 25 patients with latent syphilis whose fluids showed no other abnormality by routine tests. There appears to be a progressive rise in the titre of the immobilizing antibody from early to late syphilis, but no correlation was found between this and the reagin titre of standard tests in individual cases. It has been shown that these two antibodies are distinct by absorbing reagin from a serum with a flocculation antigen; this process does not affect the immobilizing antibody titre. The latter antibody was also found to be remarkably stable to heat, and exposure of a serum to a temperature which destroys reagin has no effect on the immobilizing antibody.

Examination of sera giving reactions of the biological false positive type has yielded interesting results. Mohr and others (1950) applied the test to patients from their private practice, who could therefore be observed under optimum conditions. Among 66 patients who, on clinical grounds, were thought to have probable late latent syphilis, the test was positive in fifty and negative in sixteen. In 63 patients whose positive serum reactions were thought to be of biological false positive type, the immobilization test was positive in only six.

Experience with other treponematoses is limited at present, but it has been found that immobilizing antibody is produced regularly as a result of infection with *T. pertenue* and with *T. cuniculi*, but not in animals receiving the non-virulent treponemata which can be grown on artificial media, such as the Reiter, Kazan, and S-26 strains. This observation supports the view that these strains are not *T. pallidum*.

The immobilization test should be a most useful technique for exploring problems of immunity

* Using a more sensitive technique, Thompson and Magnuson (1951) found only 3.3 per cent. negative immobilization tests in 152 cases of secondary syphilis.

in syphilis, both in man and in the experimental animal. Its most immediate practical application would seem to be in the investigation of patients suspected of giving biological false positive results with serum tests for syphilis. Unfortunately, in its present state it presents formidable technical difficulties which will restrict its performance to a few highly specialised serological laboratories. Tests can only be carried out on a small number of sera at once, and it will therefore be some time before sufficient experience can be gathered to define its potentialities. It is obviously, however, a major advance in the serology of treponematoses, and future developments will be eagerly awaited.

REFERENCES

- Durel, P., Sausse, A., Collart, P., Roiron, V., and Borel, L. J. (1951). *Proph. anti vénér.*, **23**, 59.
- Magnuson, H. J., and Thompson, F. A. (1949). *J. vener. Dis. Inform.*, **30**, 309.
- Mohr, C. F., Moore, J. E., Nelson, R. A., and Hill, J. H. (1950). *Amer. J. Syph.*, **34**, 405.
- Nelson, R. A. (1948). *Amer. J. Hyg.*, **48**, 120.
- , and Mayer, M. M. (1949). *J. exp. Med.*, **89**, 369.
- , Zheutlin, H. E. C., Diesendruck, J. A., and Austin, P. G. M. (1950). *Amer. J. Syph.*, **34**, 101.
- Thompson, F. A., and Magnuson, H. J. (1951). *Ibid.*, **35**, 21.
- Vaisman, A., and Hamelin, A. (1951). *Proph. anti vénér.*, **23**, 79.