THE V.D.R.L. TEST*

SIGNIFICANCE OF "ROUGH" RESULTS

BY

M. F. GARNER AND N. M. GRANTHAM

*Institute of Clinical Pathology and Medical Research,
Department of Public Health, Sydney, Australia*

During the past few decades many flocculation tests have been developed for use in the serological diagnosis of syphilis. Of these the one most widely used at the present time is the Venereal Disease Research Laboratory (VDRL) test, described by Harris, Rosenberg, and Riedel (1946) and Harris, Rosenberg, and Del Vecchio (1948) and named after the laboratory in which it was developed. The VDRL test can be performed either on a slide or in a tube, qualitatively or quantitatively. It can be carried out on serum or cerebrospinal fluid. It is undoubtedly the most useful screening test for syphilis available to-day; it is quick and easy to perform and requires a very small amount of serum or cerebrospinal fluid. In our laboratory the VDRL test does tend to be oversensitive, but as previously pointed out (Garner, 1966) this is no real drawback, especially when one test only is used to screen serum or cerebrospinal fluid and reference laboratory facilities are available for confirmation of results.

In this study particular attention was paid to what are called "rough" reactions. These are tests in which the antigen particles are seen, at $\times 100$ magnification, as single rods as well as a few irregular clumps of two or three rods in the one microscopic field. There is a distinct difference microscopically between "rough" clumps and the small even clumps which are reported as weakly reactive. It is normal to report tests showing this roughness as non-reactive.

Material and Methods

The VDRL slide test was performed as described in the U.S. Public Health Service Manual of "Serologic Tests for Syphilis" (1964). The tests were read and reported as described in this Manual.

All sera giving rough results to the VDRL slide test and non-reactive results to the cardiolipin Wassermann reaction (CWR) and the Reiter protein complement-fixation (RPCF) test were set aside and stored

at -20° C. until thawed for further investigation. The *Treponema pallidum* immobilization (TPI) test was then carried out on each serum and the results correlated with the patient's history. Where a patient's serum gave a reactive TPI test result and there was no definite history that the patient might have or have had syphilis, the TPI test was repeated to confirm the result.

The TPI test was also performed on 500 sera which gave non-reactive results to the VDRL slide, CWR, and RPCF tests. This was the control group. These sera were from patients who had no history of syphilis and showed no clinical signs suggestive of the disease.

Over the past 18 months, 61,000 sera have been tested; 514 of them gave a rough result to the VDRL slide test. This report concerns these 514 sera. These had come from people in mental hospitals, public hospitals, gaols, child welfare centres, the Army, and from patients attending venereal disease clinics; in addition some specimens had been submitted by general practitioners and pathologists. There was no difference in the origin of the sera which were reactive to the TPI test and those which were not. A reactive TPI test result was taken to indicate venereal syphilis, as this was the only treponemal disease known in the areas from which the specimens originated.

Results

Of the 514 sera examined, 325 (63.2 per cent.) were non-reactive and 189 (36.8 per cent.) reactive to the TPI test. The control group of 500 sera, which had given non-reactive VDRL slide, CWR, and RPCF test results, also gave negative results to the TPI test (see Table I).

TABLE I
COMPARISON OF VDRL AND TPI TEST RESULTS
ON 1,014 SERA

VDRL Results	TPI Reactive		TPI Non-Reactive		Total
	No.	Per cent.	No.	Per cent.	
Rough	189	36.8	325	63.2	514
Non-reactive	—	—	500	100	500

The 189 sera which gave positive results to the TPI test consisted of 72 (38.1 per cent.) from

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patients known to have had syphilis, and 117 (61.9 per cent.) from patients whose histories suggested a wide variety of disorders but who were not known to have had syphilis.

The clinical histories of the patients from whom the sera were taken could be divided into several categories:

(1) *Definite Syphilis* Sera from 100 patients were in this group. Of the 28 patients whose sera were non-reactive to the TPI test, fifteen were known to have been treated cases of primary, and one of secondary syphilis. The stage of the disease in the remaining patients was not stated, though presumably they had been treated within the first year after infection as their sera gave non-reactive TPI test results.

(2) *Suggestive of Syphilis* This included 39 patients with penile sores (results of dark-ground examination not stated), venereal warts, rashes, aortic aneurysm, Argyll Robertson pupils, ataxia, Charcot's arthropathy, and a family history of syphilis.

(3) *Possible Venereal Origin* Placed in this group were 77 patients who had had gonorrhoea, urethral or vaginal discharges, Reiter's disease, or exposure to possible infection. Sera from seventeen of 27 patients with a history of exposure to possible infection were reactive to the TPI test.

(4) *Biological False Positive Conditions* Conditions which can be associated with biological false positive reactions to reagin tests were encountered in 65 patients in this survey. These included pregnancy, recent small-pox vaccination, diabetes, lupus erythematosus, tuberculosis, and carcinoma. Pregnancy accounted for 45 of the total group, sera from seven of these patients being reactive to the TPI test.

(5) *Miscellaneous Group* This covered sera from nineteen patients with a wide variety of conditions, such as headache, renal colic, abdominal pain, pulmonary oedema, 6th nerve palsy, and patients who were pale, paranoid, or incontinent, or were being examined for admission to a home for the aged.

(6) *Reactive Screen Test Result* In this category were 21 sera referred from other laboratories with no information about the patient except that his serum had given a reactive result to a screening test for syphilis.

(7) *No Information* No data were supplied with the sera from 26 patients.

(8) *Routine Test Only* This was requested on 167 sera received.

The findings in each of these groups as well as in those sera which gave reactive and non-reactive results to the TPI test are shown in Table II.

TABLE II
TPI TEST RESULTS RELATED TO CLINICAL HISTORY ON 514 SERA GIVING "ROUGH" VDRL TEST RESULTS

History	Total Sera	TPI Results	
		Non-Reactive	Reactive
Definite syphilis	100	28	72
Suggestive of syphilis	39	31	8
Possible venereal origin	77	50	27
B.F.P. Conditions	65	53	12
Miscellaneous	19	13	6
Reactive screen test result	21	18	3
No information	26	16	10
Routine test	167	116	51
Total	514	325	189

Discussion

The TPI test is generally accepted as the most specific test available to-day for the diagnosis of treponemal disease (Wilkinson and Rayner, 1966). In this survey the treponemal disease involved is venereal syphilis, as the sera came from people living in an area where this is the only known treponemal infection. It is usual to report the results on sera showing rough reactions to the VDRL slide test, as non-reactive.

As a result of performing the TPI test on 514 sera which had given rough results to the VDRL slide test and non-reactive results to the CWR and RPCF tests, 189 of those from whom these sera were taken were shown to have had syphilis. Investigation of the histories of these patients revealed that 72 were known and 117 were not known, at least to their present medical adviser, to have had syphilis.

It is reasonable to assume that those who were not known to have had syphilis, had at some time been treated for the disease, either intentionally or unintentionally, as penicillin given for any cause will affect the course of a concurrent syphilitic infection. A less likely explanation is that in some cases infections were of such long standing that the CWR and RPCF test results had faded naturally.

It is to be expected that sera from patients with conditions known to be associated with biological

false positive reactions to reagin tests, will also give a proportion of rough results to the VDRL slide test. However, as this survey has shown, some of these patients may also have had syphilis.

It would appear to be worthwhile, where facilities exist, to investigate sera which give only a rough VDRL slide test result. The results of the TPI test on these sera could certainly help a medical adviser in assessing his patient's condition.

Summary

TPI tests were performed on 514 sera which gave rough results to the VDRL slide test and non-reactive results to the CWR and RPCF tests. It is usual to report sera giving rough VDRL slide tests results as non-reactive.

Reactive results to the TPI test were obtained on 189 of these sera, 61.9 per cent. of which came from patients not known to have had syphilis. The clinical histories of the patients in the survey are discussed.

Sera from 500 patients with no history or clinical signs of syphilis gave non-reactive results to VDRL slide, CWR, RPCF, and TPI tests.

A rough VDRL slide test result has therefore some significance, as a proportion of sera giving this reaction also give a reactive result to the TPI test. It is therefore worthwhile to perform a TPI test on all such sera, especially if the patient is not known to have had syphilis.

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REFERENCES

- Garner, M. F. (1966). *Med. J. Aust.*, **2**, 328.
 Harris, A., Rosenberg, A. A., and Del Vecchio, E. R., (1948). *J. vener. Dis. Inform.*, **29**, 72.
 —, —, and Riedel, L. M. (1946), *Ibid.*, **27**, 169.
 U.S.P.H.S. (1964). "Serologic Tests for Syphilis: 1964 Manual", rev. ed. P.H.S. Publ. No. 411. U.S. Communicable Disease Center. Government Printing Office, Washington.
 Wilkinson, A. E., and Rayner, C. F. A. (1966), *Brit. J. vener. Dis.*, **42**, 8.

Le test V.D.R.L. et la signification des résultats incomplets

RÉSUMÉ

514 spécimens de sérum qui avaient donné des résultats incomplets au test V.D.R.L. slide et des résultats non-réactifs aux tests CWR et RPCF ont subi le test TPI. Il est normal de dire que les sérums qui donnent des résultats incomplets au test V.D.R.L. slide sont non-réactifs.

Des résultats réactifs au test TPI ont été obtenus avec 189 de ces sérums, 61,9 pour cent d'entre eux venaient de sujets qu'on ne savait pas avoir été atteints de syphilis. L'historique clinique de ces sujets compris dans cette étude est discutée.

Le sérum de 500 malades ne donnant aucun passé syphilitique ou des signes cliniques de cette maladie a donné des résultats non-réactifs aux tests V.D.R.L. slide, CWR, RPCF, et TPI.

Un résultat incomplet au test V.D.R.L. a ainsi quelque signification, car une proportion des sérums donnant ce genre de réaction a aussi donné un résultat réactif au test TPI. Il vaut ainsi la peine de faire le test TPI sur tous ces sérums surtout si on ne sait pas que le malade a eu la syphilis.