Quantitation of a slide test (Monotest) for infectious mononucleosis

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SYNOPSIS A slide test for infectious mononucleosis using formalinized horse erythrocytes (Monotest2) was quantitated and compared with standard differential heterophile (Davidsohn) titres performed on the same specimens. The Monotest titre parallels the standard presumptive heterophile (antisheep cell) titre in the degree of elevation, with a ratio of Monotest to heterophile titre of approximately 1 to 56. The simplicity of the quantitative slide test recommends it as a routine test for infectious mononucleosis.

A number of new slide tests using horse erythrocytes for infectious mononucleosis have recently been introduced. These have been shown to have a high degree of sensitivity and specificity, whether the horse erythrocytes are citrated (Monospot, Ortho) (Lee, Davidsohn, and Panczyszyn, 1968) or formalin-treated (Monotest) (Hoff and Bauer, 1965; Davidsohn, 1967; Sinay, Schoen, and Miyahira, 1968; Lowell and Kazakaitis, 1969). None has mentioned quantitation of the test, and we elected to compare quantitations of the Monotest with standard differential heterophiles performed on the same serum samples.

Methods

Doubling dilutions of patients’ sera in saline were prepared using 0.25 ml volumes of serum and saline and a single 1 ml plastic disposable pipette. The Monotest was then performed according to the instructions of the manufacturer. A drop of serum dilution and a drop of Monotest reagent were mixed on a glass slide and gently rotated for two minutes. A coarse 4+ agglutination was considered positive.

Received for publication 13 February 1970.
1Please send requests for reprints to Dr Carter at Mount Sinai Hospital.
2Monotest, Wampole Laboratories.
of the tests with the clinical status of the patients; our primary consideration was a comparison of the quantitative slide test with the titres of the standard method of Davidsohn and Nelson (1969).

All of the sera were inactivated at 56°C for 30 minutes before testing.

When performing differential heterophile tests, we routinely use as reagent controls a positive control mononucleosis serum and a negative control commercial 'Forssman antibody' (serum sickness) serum. The latter is used to demonstrate the ability of the guinea pig antigen reagent to absorb heterophile antibodies other than those of infectious mononucleosis. Several lots of such commercial 'negative control' sera were included in the Monotest/Davidsohn comparison, and because of results to be described, the negative control sera were also tested with the Monospot test, performed according to the manufacturers' instructions (Monotest batch no. 73, Monospot batch no. IM-161).

**Results**

Table I presents a summary of the results. In all cases the Monotest and differential heterophile titres agreed regarding the diagnosis.

The most significant finding is that the Monotest titre generally parallels the heterophile titre. Comparison of the Monotest titre with the presumptive heterophile (antisheep cell) titre reveals a ratio of approximately 1 to 56, that is, the Monotest titre multiplied times 56 approximately equals the sheep cell titre. This value is selected, although the correlation is not perfect at all high and low titres, to enable an easy comparison of the Monotest titre values with the well known Davidsohn titre values, such that the approximate equivalent Davidsohn titre value may be reported to the physician as well as the Monotest titre, if desired.

Most of the heterophile titres were clustered about a most frequent titre +1 dilution at each level of Monotest titre, both for the unabsorbed sheep cells and after absorption with guinea-pig kidney and beef erythrocytes. In only three instances was any titre more than two dilutions from the most frequent titre. Each of the three patients had differential test titres concordant with the Monotest result.

Table II details the 'weakly reactive' Monotest reactions of undiluted (1:1) sera observed in seven of the 126 patients. None of these seven undiluted (1:1) sera showed a 4+ reaction. Results cannot be adequately interpreted, as the clinical state of the patients was not studied in depth. However, it is apparent that occasional 'doubtful' reactions occur, as in previous studies, suggesting that the test be repeated later to demonstrate a rising (or falling) titre (Sinay et al, 1968).

**Table I** Comparison of quantitative Monotest and differential heterophile titres in 126 specimens from patients

<table>
<thead>
<tr>
<th>No. of Specimens</th>
<th>Monotest Titre</th>
<th>Differential Heterophile Titre¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sheep Cell</td>
<td>Guinea-pig Kidney</td>
</tr>
<tr>
<td>23</td>
<td>Neg.</td>
<td>14</td>
</tr>
<tr>
<td>7</td>
<td>1:1</td>
<td>28</td>
</tr>
<tr>
<td>9</td>
<td>1:2</td>
<td>112</td>
</tr>
<tr>
<td>9</td>
<td>1:4</td>
<td>224</td>
</tr>
<tr>
<td>21</td>
<td>1:8</td>
<td>224</td>
</tr>
<tr>
<td>22</td>
<td>1:16</td>
<td>448</td>
</tr>
<tr>
<td>27</td>
<td>1:32</td>
<td>896</td>
</tr>
<tr>
<td>5</td>
<td>1:64</td>
<td>1792</td>
</tr>
<tr>
<td>2</td>
<td>1:128</td>
<td>3584</td>
</tr>
<tr>
<td>1</td>
<td>1:256</td>
<td>1792</td>
</tr>
</tbody>
</table>

¹Reciprocal of most frequent titre value.

**Table II** 'Weakly reactive' Monotests

Atypical beef cell absorption perha ps due to decreased antigenicity of the beef erythrocytes.

Results of the 'negative control' sera and two batches of 'positive control' commercial sera are listed in Table III.

Both the Monotest and the Monospot tests were in agreement with the differential heterophile interpretation using these sera, with one exception. The BBL serum sickness control serum, which was negative for Monospot and Davidsohn tests, revealed a fairly strong agglutination with Monotest (1:2 and 1:4, with two batches of the control serum). The reason for this is unexplained and warrants further study, as it may represent decreased specificity of the Monotest formalinized horse cells.
Table III  Slide tests for mononucleosis and Davidsohn differential test with commercial reagent control sera

<table>
<thead>
<tr>
<th>Batch No.</th>
<th>Control Serum</th>
<th>Monospot</th>
<th>Monotest</th>
<th>Presumptive</th>
<th>Guinea-pig Kidney</th>
<th>Beef RBC</th>
<th>Davidsohn Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1518320</td>
<td>Difco infectious mononucleosis-positive serum</td>
<td>Pos.</td>
<td>Pos. (1:16)</td>
<td>1:448</td>
<td>1:224</td>
<td>0</td>
<td>Pos.</td>
</tr>
<tr>
<td>804174</td>
<td>BBL positive control serum</td>
<td>Pos.</td>
<td>Pos. (1:8)</td>
<td>1:224</td>
<td>1:112</td>
<td>0</td>
<td>Pos.</td>
</tr>
<tr>
<td>9041701</td>
<td>BBL serum sickness control serum</td>
<td>Neg.</td>
<td>Pos. (1:2)</td>
<td>1:28</td>
<td>0</td>
<td>0</td>
<td>Neg.</td>
</tr>
<tr>
<td>9051711</td>
<td>BBL serum sickness control serum</td>
<td>Neg.</td>
<td>Pos. (1:4)</td>
<td>1:28</td>
<td>0</td>
<td>0</td>
<td>Neg.</td>
</tr>
<tr>
<td>8031731</td>
<td>BBL high titre heterophile normal serum</td>
<td>Q.N.S.</td>
<td>Neg.</td>
<td>1:56</td>
<td>0</td>
<td>1:56</td>
<td>Neg.</td>
</tr>
<tr>
<td>9051721</td>
<td>BBL high titre heterophile normal serum</td>
<td>Neg.</td>
<td>Neg.</td>
<td>1:56</td>
<td>0</td>
<td>1:112</td>
<td>Neg.</td>
</tr>
<tr>
<td>528219</td>
<td>Difco heterophile Forssman antiserum</td>
<td>Neg.</td>
<td>Neg.</td>
<td>1:56</td>
<td>0</td>
<td>1:28</td>
<td>Neg.</td>
</tr>
</tbody>
</table>

Discussion

For diagnostic problems that may be resolved by demonstration of rising titres, or occasionally falling titres, the quantitation of infectious mononucleosis serology could be significant. Many clinicians request quantitations of titre as an aid to management of the patient, eg, when to send the patient back to school. Previously, the recommendation has been made that when the Monotest is positive the quantitative differential absorption test might be necessary 'for obtaining titres of positivity when these are required for comparative purposes' (Davidsohn, 1967). The simple quantitation of the Monotest described here appears to be equally satisfactory if such comparative data are requested.

The results in our series indicate an apparent sensitivity and specificity of a degree similar to previous reports. As a result of these studies we now routinely perform only the Monotest, and, if positive, quantitate the specimen. We report the Monotest titre and the approximately equivalent presumptive Davidsohn (antisheep cell) titre. The differential test is reserved for special instances, as for example when the clinical status of the patient is discordant with the Monotest result, or serum sickness is considered in the differential diagnosis.

No attempt was made to test the sera without inactivation because of previous experience showing occasional false-negative reactions on unheated sera (Sinay et al., 1968). Other investigators are also inactivating their test sera (Lowell and Kazakaitis, 1969). The directions for Monotest state that the test may be performed on fresh or inactivated serum.

References

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doi: 10.1136/jcp.23.8.700

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