Evaluation of 12 Commercial Tests for Detection of Epstein-Barr Virus-Specific and Heterophile Antibodies

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Ten microbiological departments in Norway have participated in a multicenter evaluation of the following commercial tests for detection of Epstein-Barr virus (EBV)-specific and heterophile antibodies: CAPTIA Select viral capsid antigen (VCA)-M/G/EBNA (Centocor Inc.), Enzygnost anti-EBV/immunoglobulin M (IgM) and IgG (Dade Behring), Vironostika EBV VCA IgM/IgG/EBNA enzyme-linked immunosorbent assay (ELISA) (Organon Teknika), SEROFLUOR immunofluorescence assay and EBV Combi-Test (Institute Virion Ltd.), anti-EBV recombinant IgM- and IgG-early antigen/EBNA IgG ELISA (Biotest Diagnostics), EBV IgM/IgG/EBNA ELISA (Gull Laboratories), Paul-Bunnell-Davidsohn test (Sanofi Diagnostics Pasteur), Monosticon Dri-Dot (Organon Teknika), Avitex-IM (Omega Diagnostics Ltd.), Alexon Serascan infectious mononucleosis test (Alexon Biomedical Inc.), Clearview IM (Unipath Ltd.), and Cards±OS Mono (Pacific Biotech, Inc.). The test panel included sera from patients with primary EBV infection, immunocompromised patients with recent cytomegalovirus infection, healthy persons (blood donors), and EBV-seronegative persons. Among the tests for EBV-specific antibodies the sensitivity was good, with only small differences between the different assays. However, there was a greater variation in specificity, which varied between 100% (Enzygnost) and 86% (Biotest). Tests for detection of heterophile antibodies based on purified or selected antigen (Avitex, Alexon, Clearview IM, and Cards±OS Mono) were more sensitive than the Paul-Bunnell-Davidsohn and Monosticon tests.

The diagnosis of infectious mononucleosis is usually based on typical clinical and hematologic findings and confirmed with a positive test for heterophile antibodies. However, in some cases there is a need for analysis of Epstein-Barr virus (EBV)-specific antibodies, especially when there are atypical symptoms or in the absence of heterophile antibodies. This is often observed with specimens from children, who also may have an unusual EBV antibody pattern. Tests used for the virological diagnosis of mononucleosis should have both high sensitivity and high specificity.

In Norway, tests for detection of both EBV-specific and heterophile antibodies are performed at the majority of the microbiological laboratories. Our regular quality assessment system has revealed the need for better control with the use of commercial tests. Also, over the past few years, some newly developed tests have been introduced. Together with nine other microbiological laboratories, the Department of Virology at the National Institute of Public Health (NIPH) in Oslo, Norway, conducted an evaluation of a total of 12 commercial tests for detection of EBV-specific and heterophile antibodies.

MATERIALS AND METHODS

Participants in the study. The microbiological departments in the following counties in Norway participated in the study: Aust- and Vest-Agder, Akershus, Bergen, Nordland, Oslo (NIPH, the National Hospital, and Ullevål Hospital), Rogaland, Sogn and Fjordane, and Vestfold.

Tests evaluated. Table 1 gives information on the EBV serological tests evaluated, including manufacturers, antigens, test principle, and mode of detection. All enzyme-linked immunosorbent assay (ELISA) tests were based on microwell enzyme immunoassay (EIA). Table 2 gives similar information on tests for heterophile antibodies.

Test panel. A test panel consisting of 248 and 241 serum specimens for the EBV antibody and heterophile antibody evaluations, respectively, was selected on the basis of both clinical diagnosis and results of laboratory investigations. Before distribution to the sites, the sera received code numbers. Specimens were assigned to the following groups.

(i) Group A. Group A consisted of specimens from patients with recent primary EBV infection. The diagnosis was confirmed by a positive test for heterophile antibodies and an EBV antibody pattern compatible with recent primary infection. A total of 139 and 140 serum specimens were tested for EBV-specific and heterophile antibodies, respectively.

(ii) Group B. Group B consisted of eight serial dilutions (1:10, 1:20, 1:40, 1:80, 1:160, 1:320, 1:640, and 1:1,280) of serum from a patient with recent primary EBV infection. The purpose was to register eventual differences in the level of sensitivity between different tests, in particular for the various immunoglobulin M (IgM) tests for EBV-specific antibodies. The dilutions were prepared at the Department of Virology, NIPH, before distribution to the laboratories. Undiluted serum was not investigated.

(iii) Group C. Group C included 23 serum specimens from immunocompromised patients with current cytomegalovirus (CMV) infection. In this group, detection of CMV pp65 antigen in leukocytes was the criterion for selection.

(iv) Group D. Group D included serum specimens from 40 healthy persons (blood donors) age 18 to 67 years.

Group E. Group E consisted of 38 sera from patients with no previous EBV infection. These specimens were mainly from small children for whom an EBV infection is usual.
viral capsid antigen (VCA) IgG immunofluorescence test (EBV VCA IgG immunofluorescence assay [IFA] Kit II; Organon Teknika) was performed to determine past EBV infection. The serum specimens were stored at 2–20°C for about 4 months prior to testing. None of the specimens were hemolytic, and repeated freezing or thawing (more than two times) was avoided. The samples were stored at 4°C during the evaluation.

Performance of the analysis. A plan for the performance of the analysis was designed before the evaluation was started. Each site was to perform one test set for EBV-specific antibodies and one test for heterophile antibodies. In this way the sera were investigated only once in each test. The tests chosen for the individual sites were those in routine use or with which the site had some experience.

All investigations were performed between September 1997 and February 1998. The tests were performed in accordance with the manufacturer’s instructions, but analyses of sera yielding borderline results were not repeated. All of the tests were performed manually. The results of the analysis were collected and statistically evaluated at the Department of Virology, NIPH.

RESULTS
For evaluation of the results, generally accepted criteria for antibody patterns, also referred to in the manufacturers’ instructions, were used. These criteria are stated in Table 3. In addition, weak positive results (+) and borderline results (+/−) for EBV IgM and borderline results (+/−) for heterophile antibodies were considered positive for group A but were considered negative for groups C, D, and E.

Group A: patients with recent primary EBV infection. A total of 127 serum samples (91%) showed antibody patterns compatible with recent primary EBV infection for all tests. Results for 12 sera with discordant results are presented in Table 4. Virion and Biotest showed antibody patterns compatible with recent primary EBV infection for all sera in group A.

TABLE 1. Tests for EBV-specific antibodies

| Test                                      | Manufacturer   | Antibody detection | Test principle, antigen source, and mode of detection |
|-------------------------------------------|----------------|--------------------|-------------------------------------------------------|
| CAPTIA Select VCA-M/G/EBNA               | Centocor Inc.  | VCA, EBNA          | VCA IgM, μ-capture EIA; VCA and EBNA IgG, indirect EIA; conjugate, biotinylated synthetic peptide from the p18 protein and peroxidase-labeled streptavidin; qualitative detection |
| Enzygnost anti-EBV/IgM and IgG           | Behringwerke   | Combination of VCA, EA, and EBNA | Indirect EIA; antigen, combination of EBV-specific epitopes; detection of IgM and IgG antibodies, respectively, with peroxidase-labeled anti-human IgM and IgG; control antigen is included; qualitative and quantitative detection |
| Vironostika EBV VCA IgM/IgG/EBNA ELISA   | Organon Teknika| VCA, EBNA          | VCA IgM, μ-capture EIA; conjugate, monoclonal anti-VCA p18 labeled with peroxidase; synthetic VCA p18 peptide antigen is added to the conjugate diluent; VCA and EBNA IgG, indirect EIA; coating with synthetic p18 peptide antigen; qualitative and semiquantitative detection |
| SEROFLUOR IFA and EBV Combi-Test         | Institute Virion Ltd. | VCA (SEROFLUOR), VCA, EA, EBNA (EBV Combi-Test) | For SEROFLUOR, indirect IFA; antigen source, P3HR-1 cells, for EBV Combi-Test, anti-complement IF antigen source, a β-lymphocyte cell line which expresses VCA, EA, and EBNA; differentiation of VCA and EBNA antibodies is based on different reading pattern; qualitative detection |
| Anti-EBV recombinant IgM and IgG EA/EBNA IgG ELISA | Biotest Diagnostics | EA, EBNA | Indirect EIA with recombinant antigen; EA p54 and p138 for EA IgM/IgG and EBNA-1 p-172; qualitative and semiquantitative detection |
| EBV IgM/IgG/EBNA ELISA                   | Gull Laboratories | VCA, EBNA         | Indirect EIA; antigen source for VCA IgM/IgG, gp125 cultivated in P3HR-1 cells; for EBNA IgG, recombinant antigen corresponding to the C-terminal part of the EBNA-1 gene product (without IR3); qualitative detection |

TABLE 2. Tests for heterophile antibodies

| Test                                      | Manufacturer     | Test principle                                                                 |
|-------------------------------------------|------------------|-------------------------------------------------------------------------------|
| Paul-Bunnell-Davidsohn test               | Sanofi Diagnostics Pasteur | Agglutination of horse red blood cells by presence of heterophile antibodies; absorption with Forssmann antigen and bovine red blood cell emulsion |
| Monosticon Dri-Dot                        | Organon Teknika  | Latex agglutination based on erythrocyte antigen from horse and sheep; absorption with guinea pig kidney extract |
| Avitex-IM                                  | Omega Diagnostics Ltd. | Latex agglutination based on reaction with bovine erythrocyte glycoprotein |
| Alexon Serascan infectious mononucleosis test | Alexon Biomedical Inc. | Latex agglutination based on selected erythrocytes from horse |
| Clearview IM                               | Unipath Ltd.     | Direct particle-bound antigen-antibody reaction with latex-coated bovine erythrocyte glycoprotein |
| Cards±OS Mono                              | Pacific Biotech, Inc. | Color immunochromatographic assay; extracted beef stroma is immobilized on the membrane of the reaction unit (solid phase), and goat anti-human IgM antibody is linked to alkaline phosphatase |
TABLE 3. Generally accepted criteria for EBV antibody patternsa

| Condition                      | EBV antibody patterns usually obtained | Test for heterophile antibodies |
|--------------------------------|---------------------------------------|---------------------------------|
| Primary EBV infection          | +/+-/-, +/+-/-, -/+/-, +/+/-          | +                               |
| Earlier EBV infection          | -/+/-, -/+/- (for Biotest)            | -                               |
| EBV reactivation               | +/+/-/+b, +/-/+ (for Biotest)         | -                               |

a The order of the analysis is VCA/EA IgM, VCA/EA IgG, and EBNA IgG.
b Similar antibody patterns due to primary infection and reactivation may occur.

In tests for heterophile antibodies, 107 of 140 sera yielded discordant results. Results for the 33 specimens with discordant results are presented in Table 5. One serum specimen gave negative results in all tests.

A considerable variation in the results was observed. Far more negative results were obtained with the Paul-Bunnell-Davidsohn and Monosticon analyses than with the other tests.

**Group B: serial dilutions of serum from a patient with recent primary EBV infection.** Group B included serial dilutions, in phosphate-buffered saline, of serum from a patient with infectious mononucleosis. The results are shown in Table 6. There was a great variation in the ability to detect antibodies in serial serum dilutions. With Vironostika, only VCA IgG could be detected. Virion had a low sensitivity for EBNA IgG antibodies, whereas Biotest was negative for early antigen (EA) IgM and EA IgG from the dilutions 1:20 and 1:40, respectively, onwards. Test results for heterophile antibodies were not validated for sera belonging to this group.

**Group C: 23 serum specimens from immunocompromised patients with current CMV infection.** Group C comprised sera from 23 immunocompromised patients with current CMV infection. Table 7 gives a summary of the results. With the exception of serum from one patient who was seronegative, all sera met the criteria for earlier EBV infection. Vironostika and Virion gave several negative EBNA IgG results, leading to an antibody pattern which could be interpreted as a primary infection. One specimen was EBNA negative in all tests, and VCA IgM was positive in Captia and Vironostika. Since it cannot be ruled out that the patient was in a convalescent phase of mononucleosis, this specimen was considered inconclusive and was excluded from the specificity calculations.

| Serum no. | Paul-Bunnell-Davidsohn test | Monosticon | Avitex | Alexon | Clearview | Cards±OS |
|-----------|-----------------------------|------------|--------|--------|-----------|----------|
| 130       | -                           | +          | -      | -      | -         | -        |
| 131       | -                           | +          | +      | +      | +         | -        |
| 132       | +                           | +          | +      | +      | +         | +        |
| 133       | -                           | -          | -      | +      | -         | +/-      |
| 134       | +                           | -          | +      | +      | +         | +        |
| 135       | +                           | -          | +      | +      | +         | +        |
| 139       | -                           | -          | -      | -      | +/-       | +        |
| 140       | -                           | -          | -      | -      | +/-       | -        |
| 141       | -                           | +          | +      | +      | +         | +/-      |
| 176       | +                           | -          | +      | +      | +         | +        |
| 178       | +                           | -          | +      | +      | +         | +        |
| 190       | +                           | +          | -      | +      | +         | +        |
| 191       | -                           | -          | -      | +      | +         | +        |
| 192       | -                           | -          | +      | +      | +         | +        |
| 213       | -                           | +          | +      | +      | +         | +        |
| 214       | +                           | +          | +      | +      | +         | +        |
| 217       | +                           | +          | +      | +      | +         | +        |
| 226       | -                           | +          | +      | +      | +         | -        |
| 245       | -                           | -          | -      | (+)a   | -         | -        |
| 246       | +/+-                        | -          | +      | +      | +         | +        |
| 250       | +                           | +          | +      | +/+-   | -         | -        |
| 251       | +                           | +          | +      | +/+-   | -         | -        |
| 257       | -                           | +          | +      | +      | +         | +        |
| 258       | -                           | +          | +      | +      | +         | +        |
| 271       | -                           | +          | +      | +      | +         | +        |
| 291       | -                           | +          | +      | +      | +         | +        |
| 292       | -                           | +          | +      | +      | +         | +        |
| 296       | +                           | +          | +      | +      | +         | +        |
| 297       | -                           | +          | +      | +      | +         | +        |
| 300       | +                           | +          | +      | +      | +         | +        |
| 304       | -                           | +          | +      | +      | (+/-)a    | +        |
| 323       | -                           | +          | +      | +      | (+/-)a    | +        |
| 336       | -                           | -          | -      | -      | -         | -        |

a A positive reaction appeared outside the time specified by the manufacturer.

**TABLE 4. Discordant results in tests for EBV-specific antibodies for patients with recent primary EBV infection (group A)a**

| Serum no. | Captia (VCA IgM/IgG/EBNA IgG) | Enzygnost (VCA IgM/IgG/EBNA IgG) | Vironostika (VCA IgM/IgG/EBNA IgG) | Virion (VCA IgM/IgG/EBNA IgG) | Biotest (EA IgM/IgG/EBNA IgG) | Gull (VCA IgM/IgG/EBNA IgG) |
|-----------|-------------------------------|---------------------------------|-----------------------------------|-------------------------------|------------------------------|-----------------------------|
| 119       | -/-/-                         | +/±                            | -/-/-                             | -/-/-                         | +/+/+                       | +/+/+                       |
| 130       | +/±/±                         | +/±                            | -/-/-                             | -/-/-                         | +/+/+                       | +/+/+                       |
| 131       | +/±/+                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 139       | -/+/-                         | +/±                            | -/-/-                             | -/-/-                         | +/+/+                       | +/+/+                       |
| 149       | +/-/+                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 185       | +/±/+                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 188       | +/+/-                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 217       | +/+/-                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 251       | +/+/-                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 294       | +/+/-                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 336       | -/+/-                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |
| 338       | +/+/-                         | +/±                            | -/+/-                             | -/+/-                         | +/+/+                       | +/+/+                       |

a The order of the analysis is VCA/EA IgM, VCA/EA IgG, and EBNA IgG.
Group D: serum specimens from 40 healthy persons. Group D included test sera from 40 healthy blood donors. Two of them were EBV seronegative, and 17 sera gave conforming results. Table 8 gives a summary of the results for this group.

As in group C, the results revealed differences in sensitivity for EBNA IgG. Some of the tests gave negative EBNA IgG results, i.e., an antibody pattern which could be interpreted as a primary infection. Virion also had many negative EBNA IgG results in this group. Gull and Virion gave negative IgM results for all specimens belonging to this group, whereas the other tests gave positive results for all individual tests in the test set, or an antibody pattern of +/+ for Biotest, as described in Table 8. Because the sera were drawn in connection with blood donation, we suggest that this result was consistent with a reactivation rather than with a primary infection. Nonspecific reactions in the IgM tests also have to be considered. For one serum, EBNA IgG could not be detected with any of the tests, so we cannot exclude the possibility that this blood donor was in a late convalescent phase after suffering from infectious mononucleosis. This specimen was therefore not included in the calculation of specificity. Tests for heterophile antibodies were negative for all sera in this group. As the sera were investigated blind, we had no information concerning previous CMV antibody investigations for this group.

Group E: 38 sera from patients with no previous EBV infection. Group E consisted of 38 patient sera. A total of 11 sera were negative in all tests. The other sera gave one or more positive results. A summary of the results is given in Table 9.

For one serum, all tests revealed an antibody pattern which was compatible with previous EBV infection. This specimen therefore could not be regarded as negative and was excluded from the specificity calculation. For 20 specimens, at least four of the tests yielded a negative antibody pattern, and most of the tests that gave a positive result had optical density values of <200% of the cutoff value, so we suggest that nonspecific reactions may be the reason. The negative result of the other tests was therefore considered a mean value. Six other specimens gave an antibody pattern in all five ELISA tests which was considered inconclusive and were also excluded from the specificity calculation.

Two of the tests for heterophile antibodies (Alexon and Cards±Mono) gave two positive results each for the sera in group E. However, since the EBV antibody pattern did not give any evidence of current infection, these results were regarded as unspecific.

The different tests gave the following number of positive results for group E specimens (for one or several of the individual tests in the group): Captia, 6; Enzygnost, 0; Vironostika, 2; Virion, 1; Biotest, 13 (mainly EA IgM results); and Gull, 8 (mainly VCA IgG and EBNA results).

Calculation of sensitivity and specificity. (i) Tests for EBV-specific antibodies. The basis for calculation of sensitivity and specificity was as follows. A total of 139 sera belonging to group A gave antibody patterns consistent with current infection. In groups C, D, and E a total of 93 sera gave antibody patterns compatible with previous or no EBV infection, while 8 sera were excluded because of inconclusive results. The calculated sensitivities for the different tests are as follows: Captia, 97% (135/139); Enzygnost, 99% (138/139); Vironostika, 95% (132/139); Virion, 100% (139/139); Biotest, 100% (139/139); and Gull, 96% (134/139). The calculated specificities are as follows: Captia, 90% (84/93); Enzygnost, 100% (93/93); Vironostika, 89% (83/93); Virion, 87% (81/93); Biotest, 86% (80/93); and Gull, 90% (84/93).

The sensitivities were between 95 and 100%, showing a high consistency. This can probably be explained by the fact that the

| Serum no. (dilation) | Results with: |
|----------------------|--------------|
| | Captia (VCA IgM/IgG/EBNA IgG) | Enzygnost (IgM/IgG) | Vironostika (VCA IgM/IgG/EBNA IgG) | Virion (VCA IgM/IgG/EBNA IgG) | Biotest (EA IgM/IgG/EBNA IgG) | Gull (VCA IgM/IgG/EBNA IgG) |
| 259 (1:10) | +/+/+ | +/+ | −/−/− | +/+/− | +/+/+ | +/+/+ |
| 260 (1:20) | +/+/+ | +/+ | −/−/− | +/+/− | −/+/+ | +/+/+ |
| 261 (1:40) | +/+/+ | +/+ | −/−/− | +/+/− | −/+/+ | +/+/+ |
| 262 (1:80) | −/+ | ±/± | −/−/− | +/+/− | −/+/+ | +/+/+ |
| 263 (1:160) | −/+ | ±/± | −/−/− | +/+/− | −/+/+ | +/+/+ |
| 264 (1:320) | −/+ | ±/± | −/−/− | −/+ | −/+/+ | −/+ |
| 265 (1:640) | −/+ | ±/± | −/−/− | −/+ | −/+/+ | −/+ |
| 266 (1:1,280) | −/+ | ±/± | −/−/− | −/+ | −/+/+ | −/+ |

Table 6. Results of EBV serology for serial dilutions from a patient with mononucleosis (group B)

| No. determined by: | Captia (VCA IgM/IgG/EBNA IgG) | Enzygnost (IgM/IgG) | Vironostika (VCA IgM/IgG/EBNA IgG) | Virion (VCA IgM/IgG/EBNA IgG) | Biotest (EA IgM/IgG/EBNA IgG) | Gull (VCA IgM/IgG/EBNA IgG) |
|-------------------|-----------------------------|------------------|-----------------------------------|-----------------------------|----------------------------|--------------------------|
| Previous infection (−/+/+ or −/−/+) | 19 | 21 | 15 | 17 | 19 | 21 |
| EBV reactivation (+/+/+ or +/+/−) | 1 | 1 | 1 | 4 | 1 | 1 |
| Seronegative patient (−/−/−) | 1 | 1 | 1 | 1 | 1 | 1 |
| EBNA IgG negative, antibody pattern consistent with primary infection (+/−/+, +/−/−, or −/+/+) | 1 | 1 | 1 | 1 | 1 | 1 |

* Excluded from the specificity calculation.
TABLE 8. Summary of results for 40 healthy blood donors (group D)

| EBV antibody pattern compatibility | No. determined by: |
|-----------------------------------|--------------------|
|                                   | Captia (VCA IgM/IgG/EBNA IgG) | Enzygnost (VCA IgM/IgG/EBNA IgG) | Vironostika (VCA IgM/IgG/EBNA IgG) | Virion (VCA IgM/IgG/EBNA IgG) | Biotest (EA IgM/IgG/EBNA IgG) | Gull (VCA IgM/IgG/EBNA IgG) |
| Previous infection (−/+ or −/−)   | 32                  | 34                  | 24                  | 30                  | 27                  | 36                  |
| EBV reactivation (+/+ or +/−)     | 4                   | 3                   | 10                  | 2                   | 2                   | 1                   |
| Seronegative patient (−/+−)       | 2                   | 2                   | 2                   | 3                   | 7                   | 1                   |
| Antibody pattern consistent with primary infection (+/+− or +/−−) | 1 | 1 | 1 | 1 | 1 |

Inconclusive result

Table 9. Summary of results for 38 patients with no previous EBV infection (group E)

| Antibody pattern | No. determined by: |
|------------------|--------------------|
|                  | Captia (VCA IgM/IgG/EBNA IgG) | Enzygnost (VCA IgM/IgG/EBNA IgG) | Vironostika (VCA IgM/IgG/EBNA IgG) | Virion (VCA IgM/IgG/EBNA IgG) | Biotest (EA IgM/IgG/EBNA IgG) | Gull (VCA IgM/IgG/EBNA IgG) |
| −/−/−             | 25                  | 31                  | 29                  | 30                  | 18                  | 23                  |
| +/−/−             |                     |                     |                     |                     |                     | 11                  |
| −/+−              | 4                   | 2                   | 1                   | 1                   | 1                   | 6                   |
| −/−+              | 3                   | 1                   | 1                   | 1                   | 1                   | 6                   |
| +/++              |                     |                     |                     |                     |                     |                     |
| +/+−              |                     |                     |                     |                     |                     |                     |
| +/−−              |                     |                     |                     |                     |                     |                     |
| Inconclusive result* | 6 | 6 | 6 | 6 | 6 |

* Excluded from the specificity calculation.
addition to VCA IgM, as our evaluation also demonstrates (8). In this way it is possible to avoid incorrectly diagnosing EBV reactivations as primary infections. Since the patients in group C were immunosuppressed, EBNA IgG antibodies probably exist in relatively low titer, and thus a highly sensitive assay is required. When using a sensitive EBNA IgG test as a screening test, antibodies against the other EBV antigens have to be analyzed in cases of EBNA IgG-negative sera (8).

Enzygnost, which apparently has a higher specificity than the other tests, has no means of distinguishing between VCA IgG and EBNA antibodies. With positive results for IgM and IgG, it is not possible to differentiate between primary infection and reactivation. Other investigations have shown that the IgM test may give many equivocal results (8).

The Virion EBNA IgG test seems to be somewhat less sensitive than some of the other tests. In addition, the interpretation of results requires experience. Captia and Vironostika are recently developed tests, and both are based on a synthetic peptide antigen. Vironostika EBNA IgG seemed to be somewhat less sensitive than the other tests. Captia VCA IgG and EBNA IgG gave some unspecific reactions in group E.

For the purpose of detecting heterophile antibodies, Avitex and Clearview yielded the best results even though Clearview gave some borderline results for patients with recent primary EBV infection. Cards: Mono and Alexon can also be recommended. Since rapid tests are extensively used in general practice, a high specificity is important because a false-positive result can lead to an erroneous diagnosis (4). The Paul-Bunnell-Davidsohn and Monosticon tests had lower sensitivities than the other tests and cannot be recommended. A previous evaluation has also shown that tests with purified antigens have increased sensitivity and specificity compared with methods based on sheep, horse, or bovine erythrocyte agglutination (2).

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