Comparison of Immulite with Vidas for Detection of Infection in a Low-Prevalence Population of Pregnant Women in The Netherlands

F. VLASPOLDER,1* P. SINGER,1 A. SMIT,1 AND R. J. A. DIEPERSLOOT2

Laboratory for Medical Microbiology, Medical Center Alkmaar,1 and Laboratory for Medical Microbiology, Diakonessen Hospital, Utrecht,2 The Netherlands

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A comparative evaluation of the Vidas system (bioMérieux, Marcy l’Etoile, France) and the Immulite System (Diagnostic Products Corporation) was performed using 500 prospectively collected serum samples. As part of a routine antenatal screening program, these samples were tested for hepatitis B surface antigen, and immunoglobulin G (IgG) and IgM antibodies to Toxoplasma gondii and rubella virus. The overall agreement between the two assay systems ranged from 98.0 to 99.8%. After discrepancy analysis the outcome in terms of relative sensitivity and specificity varied from 97.5 to 100%.

Primary infection caused by Toxoplasma gondii or rubella virus in pregnant women can lead to congenital infection, with serious sequelae for the newborn (4). Although rubella vaccination has reduced the incidence of rubella virus infection substantially, maternal infection in industrialized countries is still estimated to occur in 1 out of 6,000 to 10,000 pregnancies (3).

Due to a high proportion of seronegative results to T. gondii during pregnancy, it is important to clearly understand the woman’s serological status in the first trimester (8). Symptoms such as chorioretinitis and delay in development of the fetus can be prevented if timely treatment with spiramycin is initiated (6). Detection of immunoglobulin M (IgM) antibodies is problematic because of the reported low degree of test specificity and the clinical implications of a false-positive result, which can lead to unnecessary therapeutic intervention.

It is therefore of utmost importance to identify susceptible pregnant women in order to offer early treatment. Screening programs for pregnant women are now available in various Western countries (9, 16). Most recently, hepatitis B has been added to the screening program since hepatitis B vaccination (passive and active) of the newborn can actually prevent transmission (14).

Antenatal screening programs produce a substantial workload for the microbiological laboratory. Testing of large numbers of serum samples has shifted in recent years, from batch processing with enzyme immunoassays to sophisticated random-access systems capable of processing a variety of tests simultaneously (2).

In this study, we compare the results of antenatal screening for T. gondii and rubella virus antibodies and HBsAg using the bioMérieux (Marcy l’Etoile, France) Vidas and Diagnostic Products Corporation (DPC) (Los Angeles, Calif.) Immulite systems.

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Materials and Methods

In June and July 1999, a total of 500 serum samples, prospectively collected from women in their first trimester of pregnancy, were tested using the Vidas (bioMérieux) and DPC Immulite systems, for the presence of HBsAg, and for IgG and IgM antibodies to rubella virus and T. gondii. Analysis of both immunoassay systems was performed according to the manufacturers’ instructions. An aliquot of 2 ml of each serum sample was frozen at −20°C for retesting and/or confirmatory procedures.

The Vidas immunoassay system is based on the enzyme-linked fluorescent assay. The DPC Immulite is a bench-top immunoassay analyzer with continuous random-access capabilities that uses enzyme-amplified chemiluminescent chemistry for antibody or antigen detection (1, 5).

If an HBsAg-reactive sample was identified, the test was repeated in duplicate and all repeat positives were confirmed using the respective manufacturer’s HBsAg confirmatory assay. Samples that yielded discrepant results in the rubella virus IgG and IgM assays were retested in duplicate on both systems. Samples with discrepant IgG results for rubella virus and T. gondii were shipped to a reference laboratory to be resolved by testing with the Abbott AxSYM system. Repeatedly discordant rubella IgM samples were retested for evaluation with an immunofluorescence assay (Virgo).

In the case of IgM-reactive results with the T. gondii assay, an avidity IgG test was performed on the Vidas system. Samples with a low-avidity IgG result were sent to a reference laboratory (Reference Institute, Academic Medical Center, Amsterdam, The Netherlands), where five additional assays (Sabin-Feldman, Abbott IMx IgG and IgM, and bioMérieux ISAGA IgG and IgM assays) were performed.

Results

Serum samples from 500 women in their first trimester of pregnancy were collected for analysis with both systems’ assays. A comparison of the respective results is presented in Table 1. The overall agreement between the two systems ranged from 98.0 to 99.8%.

HBsAg. None of the samples was found to be positive for HBsAg by either the Immulite or the Vidas system. One sample, reactive by the Immulite assay and negative by the Vidas assay, could not be confirmed by the DPC confirmatory assay; similarly another sample, reactive by the Vidas assay and negative by the Immulite assay, could not be confirmed by the Vidas confirmatory assay. There was a total agreement of 100% between the two systems after discrepancy analysis.

Toxoplasma IgG and IgM results. Our studies indicate that almost 31% of pregnant women are seropositive for T. gondii
(Table 1), and therefore, 69% are at risk of acquiring primary *T. gondii* infection.

Using the Toxoplasma IgG assays, one confirmed negative and one confirmed positive sample scored false positive and false negative, respectively, with the Vidas system, and two confirmed positive samples scored false negative with the Immulite system. In addition, resolution of one discrepant sample could not be done due to the lack of a confirmatory test result (Table 2).

In the case of IgM, the Immulite system reported 14 samples and the Vidas system reported 13 samples as positive or indeterminate (Table 3) before testing for IgG avidity. Based on the outcome of high avidity to IgG, only three cases within our test population were confirmed as IgM positive by the IgG avidity (low avidity IgG) test. Two of these samples were sent to a reference laboratory for comprehensive testing. (Because the third sample was not followed up with a second serum sample, no conclusion could be drawn.) Results from the reference laboratory confirmed that in one case there was a recent infection (Table 4). Based upon IgG avidity testing, primary infection was not indicated in any of the other IgM-positive samples.

### TABLE 1. Agreement between the Vidas and Immulite systems*

| Assay       | Positive | Indeterminate | Agreement (%) |
|-------------|----------|---------------|---------------|
| HBsAg       | 0        | 0             | 99.8          |
| RubG        | 7        | 490           | 99.4          |
| RubM        | 496      | 1             | 99.4          |
| ToxG        | 341      | 154           | 99.0          |
| ToxM        | 483      | 7             | 98.0          |

* A total of 500 serum samples was tested in each assay.

### TABLE 2. Toxoplasma IgG and rubella IgG and IgM results after discrepancy analysis

For rubella and toxoplasma IgG are given in international units per milliliter. Those for rubella IgM are indices; the Vidas assay was performed three times, and all results are listed.

#### Rubella virus IgG and IgM results
Ten women (2.0%) were consistently found, by both rubella IgG assays, to have unprotective antibody levels. One sample that was indeterminate by the Vidas system and positive by the Immulite system was confirmed as positive. A second sample reported as indeterminate by the Immulite system and found positive by the Vidas system was confirmed as positive. Three samples that were negative by the Immulite system had indeterminate results by the Vidas system. Two samples, originally reported as negative by the Immulite system, were confirmed as negative but remained indeterminate with the Vidas system after repeat testing. In the case of rubella IgM detection, one sample that was reported as negative by the Immulite system and indeterminate by the Vidas system was sent to the reference laboratory and found to be weakly positive by an immunofluorescence assay (Table 2).

### DISCUSSION
In this study, using 500 prospectively collected samples obtained from routine antenatal screening, we compared the results obtained with the Vidas and the Immulite random-access analyzers for detection of *T. gondii* IgG and IgM antibodies and HBsAg. The overall agreement between the manufacturers’ various assays was very high and ranged from 98.0 to 99.8% (Tables 1 and 5). These results are
similar to those previously reported in comparative studies (5, 11, 12, 14, 17).

Approximately 31% of our serum samples were confirmed to be positive for *T. gondii* IgG antibodies. These figures are similar to seroprevalence data from some other Western countries (5) but substantially higher than the figures reported from Scandinavian countries (9). The data from this study indicate that almost 70% of the pregnant women are seronegative and therefore at risk of acquiring primary *T. gondii* infection. Discrimination between primary *T. gondii* infection acquired in early pregnancy and infection that may have occurred prior to pregnancy can be assessed by testing the avidity of toxoplasma-specific IgG (7). Despite the high proportions of women at risk, we found only one recent infection as determined by IgM reactivity and a low IgG avidity result. IgM positivity has to be subsequently confirmed by a confirmatory method such as avidity testing (7, 10, 13). In this study, all toxoplasma IgM-positive samples with low-avidity IgG results were sent to the Reference Institute, Academic Medical Center, for further testing. All positive IgG samples with low-avidity IgG results were sent to the Reference Institute for additional testing.

After discrepancy analysis, the seroprevalence of rubella virus IgG in our test population was over 98%—typical for countries that have instituted a rubella vaccination program. In one case, a patient with no clinical symptoms or known recent rubella contact was found to be weakly positive in a confirmatory immunofluorescence assay (Immulate assay result negative and Vidas assay result indeterminate [Table 2]).

In conclusion, the performance of the Vidas and the Immulite systems was found to be equivalent for the five assays studied, with the overall agreement ranging from 98% for toxoplasma IgM to 99.8% for HBsAg (Table 5). In comparison with the Vidas system, the Immulite system has the advantage that only one serum sample has to be loaded for the five assays tested. And secondly, because of the different incubation times when using the Vidas system, the Immulite system has more random-access capabilities. Therefore, the Immulite system was found to be not only a sensitive and specific system that can be used in the laboratory for routine antenatal screening for detection of HBsAg, *T. gondii* IgG and IgM antibodies, and rubella virus IgG and IgM antibodies, but also more easy to use when a large number of samples has to be tested.

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