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# Performance Characteristics of Four High-Throughput Immunoassays for Detection of IgG Antibodies against SARS-CoV-2

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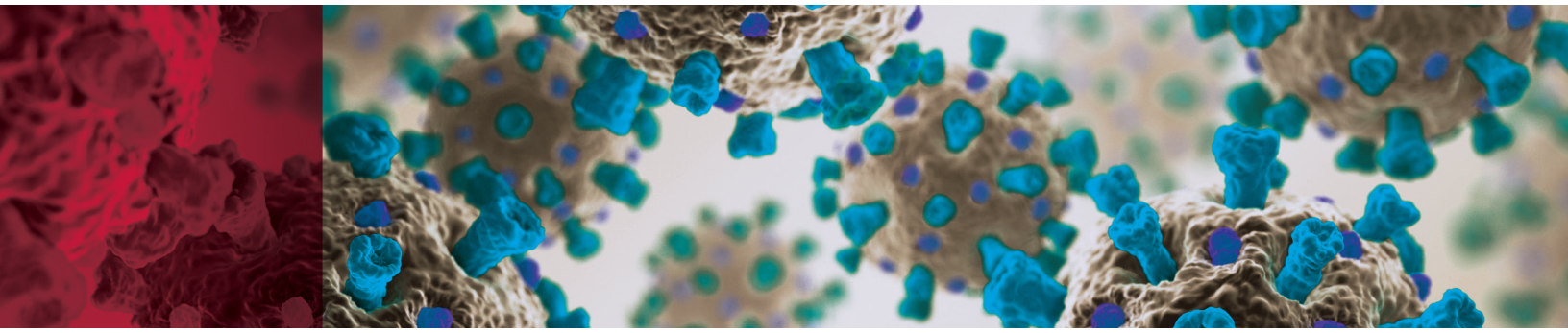
*Journal of Clinical Microbiology.* Posted online 8 June 2020 doi:10.1128/JCM.01243-20 https://jcm.asm.org/content/early/2020/06/08/JCM.01243-20



## OBJECTIVE

In response to the COVID-19 pandemic, serology tests for the detection of SARS-CoV-2 were developed and rapidly commercialized. A comparison of the performance characteristics of four high throughput serologic tests for detection of anti-SARS-CoV-2 IgG antibodies was independently performed at the Mayo Clinic, Rochester, MN. The four assays were from Abbott Laboratories, Epitope Diagnostics, Inc., Euroimmun, and Ortho Clinical Diagnostics (Ortho).

## METHODS

The sensitivity of the four assays was assessed using a panel of serially collected serum samples (n=224) from 56 patients confirmed positive for COVID-19 by a SARS-CoV-2 RT-PCR test performed on a nasopharyngeal swab. There were two patient cohorts, hospitalized patients (n=33) and those who were treated as out-patients (n=23). Sensitivity was calculated at different time points post symptom onset.

Specificity was assessed by evaluating each assay with two panels of serum samples, 149 samples from healthy adult donors collected in 2018 and 105 samples collected in January and February 2020 as part of routine clinical care. These 105 samples comprised the cross-reactivity panel (see Table 1).

## RESULTS

In the samples collected from hospitalized patients, the sensitivity ranged from 27.5% to 49.5% in samples collected 8 to 14 days post symptom onset. The assays from Ortho, Euroimmun and Epitope achieved 100% sensitivity in samples collected at least 15 days following symptom onset (see Table 2).

In the out-patient group, sensitivity ranged from 9.1 to 18.2% in samples collected seven days or less since testing positive with a SARS-CoV-RT-PCR test. Sensitivity increased significantly to 91.3% for the Euroimmun assay and to 95.7% for the Abbott and Ortho assays in samples collected 20 to 31 days after an initial positive molecular test (see table 2).

Overall specificity was calculated using the results from the healthy donor sera and the cross-reactivity panel. The Abbott, Epitope, and Ortho assays all showed a specificity of 99.6% and the Euroimmun assay 98% (see Table 3).

The Anti-SARS-CoV-2 IgG test from Ortho was one of the two highest performers on sensitivity and specificity. It also performed the best (100% specificity) on a cross-reactivity panel with multiple pathogen types.

## CONCLUSIONS

Recent publications have identified four areas of use for COVID-19 antibody tests: 1) seroprevalence and epidemiology studies 2) screening of potential convalescent plasma donors 3) assessment of candidate vaccine efficacy and 4) as an aid in diagnosis in select scenarios.*

Considering the primary use for the tests at this time is to monitor seroprevalence of the disease, it is important to use an assay with the highest specificity to maximize the Positive Predictive Value of the results. The overall accuracy of the COVID-19 serology tests is significantly impacted by both the test specificity and prevalence of the disease in the population.

Laboratories should thoroughly evaluate the accuracy of a COVID-19 serology test prior to implementation.

The role of serology testing will likely evolve as the immune response to the virus is understood, correlates of immunity are identified and the level and duration of such immunity is determined following infection or vaccination.

**Table 1:** Specimens for cross-reactivity, comprised of the 105 patient serum samples collected in January and February 2020.

| **Sera Positive for IgM and/or IgG antibodies** | |
|---|---|
| Cytomegalovirus | 15 |
| Influenza | 10 |
| Mycoplasma pneumoniae | 15 |
| Chlamydophila pneumoniae | 21 |
| Streptococcus pneumoniae urinary antigen | 12 |
| **Sera Positive by a respiratory pathogen RT-PCR panel** | |
| Commonly circulating coronaviruses | 6 |
| Influenza | 14 |
| Metapneumovirus | 4 |
| Respiratory syncytial virus | 3 |
| Adenovirus | 6 |
| Rhinovirus/enterovirus | 1 |

**Table 2:** Sensitivity (%) of four commercially available anti-SARS-CoV-2 IgG assays

| | **Serum Samples from In-Patients, Days Post-System Onset** | | | **Serum Samples from Out-Patients, Days Post First RT-PCR Positive Result** | |
|---|---|---|---|---|---|
| **Manufacturer** | **≤ 7** | **8-14** | **≥ 15** | **≤ 7** | **≥ 20** |
| **Abbott** | 10.5% (4/38) | 49.5% (45/91) | 91.8% (56/61) | 18.2% (2/11) | 95.7% (22/23) |
| **Epitope** | 2.6% (1/38) | 45.1% (41/91) | 100% (61/61) | 9.1% (1/11) | 56.5% (13/23) |
| **Euroimmun** | 0% (0/38) | 27.5% (25/91) | 100% (61/61) | 18.2% (2/11) | 91.3% (21/23) |
| **Ortho Clinical** | 2.6% (1/38) | 38.5% (35/91) | 100% (61/61) | 9.1% (1/11) | 95.7% (22/23) |

**Table 3:** Specificity (%) of four commercially available anti-SARS-CoV-2 IgG assays

| **Manufacturer** | **Healthy Donors** | **Cross-Reactivity Panel** | **Overall (95% CI)** |
|---|---|---|---|
| **Abbott** | 100% (149/149) | 99% (104/105) | 99.6% (97.6%-100%) |
| **Epitope** | 100% (149/149) | 99% (104/105) | 99.6% (97.6%-100%) |
| **Euroimmun** | 99.3% (148/149) | 96.2% (101/105) | 98% (95.3%-99.3%) |
| **Ortho Clinical** | 99.3% (148/149) | 100% (105/105) | 99.6% (97.6%-100%) |

* Select scenarios include cases with SARS-CoV-2-RT-PCR negative patients who present later in disease course and for whom collection of a lower respiratory tract sample is not possible.