Serologic Testing for IgG Antibodies Against SARS-CoV-2

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Disclosures

• None
Timing of Antibody Development After SARS-CoV-2 Infection

- New virus = no pre-existing antibodies or immunity
- We are still learning about our immune response to SARS-CoV-2
  - Many develop Abs ~1-2 weeks after symptoms
  - >95% of patients are Ab positive after 2 weeks

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- New virus = no pre-existing antibodies or immunity
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  - Many develop Abs ~1-2 weeks after symptoms
  - >95% of patients are Ab positive after 2 weeks
  - IgM declines rapidly 5-7 weeks post onset
  - IgG remains positive for ≥10 weeks post onset
- What role do serologic tests for SARS-CoV-2 play?
What Role Does Serology Play for SARS-CoV-2?

- Utilization consensus among multiple organizations (ASM, IDSA, etc.):
  - Epidemiology/prevalence studies and/or to facilitate contact tracing
  - Identification of potential convalescent plasma donors
  - Evaluation of immune response to candidate vaccines
What Role Does Serology Play for SARS-CoV-2?

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  ◦ Epidemiology/prevalence studies and/or to facilitate contact tracing
  ◦ Identification of potential convalescent plasma donors
  ◦ Evaluation of immune response to candidate vaccines
  ◦ *Potential aid for the diagnosis of COVID-19 in PCR negative patients presenting later in their disease course*

• Recommendations against use for:
  ◦ Diagnosis of acute/recent COVID-19
  ◦ Determination of whether or not a patient has developed protective immunity
  ◦ Guide Personal Protective Equipment use or adherence for social distancing practices
An Unprecedented Influx of Serologic Tests for SARS-CoV-2

- Currently: ~190 commercially available serologic tests for SARS-CoV-2
  - 12 with emergency use authorization (EUA) granted by the FDA
  - Remaining have submitted for EUA
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- 29 serologic test manufacturers either did not receive or submit for EUA
  - Test should not be distributed or used

Differences in SARS-CoV-2 Serologic Test Designs

- Format
  - Lateral Flow Assays
  - Enzyme Linked Immunosorbent Assays (ELISAs)
  - Chemiluminescent Immunoassays (CLIAs)
- Type of Antibody Detected
  - IgM
  - IgG
  - IgA
  - Total Abs
- SARS-CoV-2 Protein Used in the test
  - Spike protein – Subunit 1 and/or 2 (S1/S2)
  - Receptor Binding domain (RBD)
  - Nucleocapsid
### 12 Serologic Assays with FDA Emergency Use Authorization

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Specimen Type</th>
<th>Ab Class Detection</th>
<th>SARS-CoV-2 Protein Target</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wadsworth Center (NY)</td>
<td>Serum (S)</td>
<td>Total</td>
<td>Nucleocapsid (NC)</td>
<td>CLIA</td>
</tr>
<tr>
<td>Bio-Rad Laboratories</td>
<td>S, Plasma (P)</td>
<td>Total</td>
<td>NC</td>
<td>ELISA</td>
</tr>
<tr>
<td>Ortho-Clinical Diagnostics</td>
<td>S, P</td>
<td>Total</td>
<td>S1</td>
<td>CLIA</td>
</tr>
<tr>
<td>Roche Diagnostics</td>
<td>S, P</td>
<td>Total</td>
<td>NC</td>
<td>CLIA</td>
</tr>
<tr>
<td>Autobio Diagnostics</td>
<td>S, P</td>
<td>IgM &amp; IgG</td>
<td>Spike</td>
<td>LFA</td>
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<tr>
<td>Chembio Diagnostics</td>
<td>Finger/venous Whole Blood, S, P</td>
<td>IgM &amp; IgG</td>
<td>NC</td>
<td>LFA</td>
</tr>
<tr>
<td>Cellex Inc.</td>
<td>S, P, venous WB</td>
<td>IgM &amp; IgG</td>
<td>?</td>
<td>LFA</td>
</tr>
<tr>
<td>Abbott Laboratories</td>
<td>S, P</td>
<td>IgG</td>
<td>NC</td>
<td>CLIA</td>
</tr>
<tr>
<td>DiaSorin Inc.</td>
<td>S, P</td>
<td>IgG</td>
<td>S1/S2</td>
<td>CLIA</td>
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<td>Mount Sinai Laboratory</td>
<td>S, P</td>
<td>IgG</td>
<td>RBD</td>
<td>ELISA</td>
</tr>
<tr>
<td>Euroimmun US Inc</td>
<td>S, P</td>
<td>IgG</td>
<td>S1</td>
<td>ELISA</td>
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</table>
Performance Characteristic: Sensitivity

- Serial serum samples were collected from COVID-19 RT-PCR confirmed hospitalized patients and tested by the Ortho-Clinical anti-SARS-CoV-2 IgG CLIA

Performance Characteristic: Specificity

- Serum collected from 149 healthy donors pre-outbreak and 105 sera with antibodies to other pathogens:

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<td>Cross- Reactivity Panel</td>
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- Positive predictive value: Probability that individuals that test positive truly has antibodies to the virus
  - Impacted by test specificity and prevalence of the disease
  - The lower the prevalence, the higher the risk of a false positive result
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<td>Ortho-Clinical IgG CLIA</td>
<td>99.3% (149/150)</td>
<td>100% (105/105)</td>
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<th>1% Prevalence of COVID-19</th>
<th>5% Prevalence of COVID-19</th>
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<tr>
<td>Sensitivity</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.6%</td>
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<tr>
<td>PPV</td>
<td>71.6%</td>
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Interpretation of Results from Antibody Tests for SARS-CoV-2

- **Negative Result:**
  - *Likely* no prior infection or exposure to the virus
    - Individuals tested too soon following infection or who are significantly immunosuppressed may be negative
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• What these results *do not* (yet) tell us:
  • Whether patients/individuals are protected against re-infection
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  - What these results do not (yet) tell us:
    - Whether patients/individuals are protected against re-infection
    - Cannot use positive antibody results to guide decisions regarding adherence to social distancing recommendations, use of masks or other personal protective equipment

**What Do We Know About Protective Immunity Against Re-Infection with SARS-CoV-2?**

- Protective immunity is a multi-faceted
What Do We Know About Protective Immunity Against Re-Infection with SARS-CoV-2?

• Protective immunity is a multi-faceted
• IgG antibodies can be binding or neutralizing antibodies (NAbs)
  • NAbs independently block viral entry into host cells
  • Commercially tests do not distinguish NAbs from non-NAbs

• Testing for NAbs is challenging and requires specialized facilities
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- Testing for NAbs is challenging and requires specialized facilities
- Initial studies indicate:
  - Most individuals develop NAbs after SARS-CoV-2 infection
  - Re-infection does not occur in rhesus macaques following primary SARS-CoV-2 infection

Unknowns:
- What level of NAbs are protective?
- How long do they last (6 months, 1 year, 2 years)?
Summary and Outstanding Questions

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- Serologic assays vary in design and performance characteristics
  - IgG antibodies persists for at least 8 weeks post symptom onset
  - Performance characteristics are generally good for EUA tests
    - Potentially limited utility due to low PPV in low prevalence areas, despite high assay specificity
- Neutralizing antibody assays detect antibodies able to inactivate/inhibit virus
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• **Unknowns:** Level and duration of protective immunity against reinfection

**THANK YOU**