

## **SARS-CoV-2 Antibody Testing and Covid-19 Disease**

### **Recommendations:**

The following recommendations are provided from the Yale Medicine/Yale New Haven Health Testing Stewardship Committee based on current information and CDC guidelines from 3/17/2021 <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>

### ***Clinical Decision Making and Infection Prevention***

- Clinical decision making should not be influenced by antibody testing (i.e., serologic status) except in cases of MIS-C (multi-inflammatory syndrome in children).  
MIS-C is a serious post-infectious complication of Covid-19 in children. Covid-19 antibodies should be ordered in any pediatric patient where MIS-C is considered in the differential diagnosis.
- Antibody testing results **MUST NOT** be used to adjust infection prevention measures and behaviors (including use of PPE), determine whether vaccination is indicated in someone with prior Covid-19 infection, or inform return to work/school status after Covid-19 infections, travel, or exposures.
- Currently, CDC and IDSA **DO NOT** recommend antibody testing to assess post-vaccine immunity or the need for vaccination in an unvaccinated person. Per CDC, those with a history of Covid-19 should still be vaccinated, regardless of serology status.
- Currently there are no clinical indications for repeated antibody testing.

### **Situation:**

Guidance is needed on 1) the potential role for SARS-CoV-2 antibody testing to identify immune response from previous Covid-19 infection and following vaccination, and 2) results interpretation.

### **Background and Definitions:**

#### ***General Background***

- Following infection with SARS-CoV-2, detectable antibodies are made against 2 viral protein targets: spike (S) and nucleocapsid (N) proteins. Serologic status can be determined with antibody testing.
- The S protein contains the receptor binding domain (RBD) which can also induce measurable antibodies. Neutralizing antibodies that inhibit SARS-CoV-2 replication *in vitro* mainly target the RBD.
- All currently authorized antibody tests provide a qualitative result (positive/negative). Some tests provide a numerical result; these tests are classified as semi-quantitative by the FDA and have undergone additional procedures to allow comparability among results, though the utility of this is not known at this time.

#### ***Identifying Individuals with Prior Exposure to SARS-CoV-2***

- Positive antibody testing may aid in identifying individuals with an adaptive immune response to prior SARS-CoV-2 infection or following vaccination.

*This statement is based on current information, recommendations, and evidence and will be subject to revision or retraction based on continued monitoring by the Committee.*

- If ordering after SARS-CoV-2 infection, test a minimum of 11 days after onset of symptoms.
- If ordering, antibody testing should be performed at a high-quality laboratory.

#### ***Clarification on Viral Protein Targets of Antibody Tests***

- If ordered, antibody testing should be tailored to the clinical scenario (see Table). ***In most cases, anti-S or anti-N alone will be sufficient to address the question at hand.***
- At the time of this writing (April 2021), anti-S antibodies may occur after viral infection or after vaccination, and anti-N antibodies occur only in patients with prior infection.
  - If testing for prior infection (regardless of vaccination status), both anti-S (Full-length Spike or S1-RBD) and an anti-N antibody tests should be positive.
  - If testing after vaccination (without known prior infection), only anti-S (Full-length Spike or S1-RBD) should be positive; anti-N should be negative.

#### **Antibody Tests Are Not Used to Diagnose Acute SARS-CoV-2 Infection**

- Antibody testing should NOT be used to diagnose acute Covid-19. The gold standard for diagnosis of acute SARS-CoV-2 infection is the detection of SARS-CoV-2 RNA by amplified testing for viral RNA (such as RT-PCR).

#### **Assessment:**

1. In unvaccinated individuals, positive antibody testing with validated assays indicates prior infection and helps document prior infection in those who were not tested for viral RNA or tested negative for viral RNA. Positive antibody testing likely correlates with immune protective mechanisms, although it is not known whether this group of patients will be protected from re-infection, with particular concern for the new variant viral strains.
2. A proportion of persons infected with SARS-CoV-2 may not develop measurable antibodies. Therefore, negative antibody testing does not exclude previous infection. Also, false negative results may occur if tested less than 11-21 days post symptom onset, prior to antibody rise. Further, measurable antibodies may wane over time and those with mild infection may not produce detectable antibodies.
3. Post-vaccination antibody values that indicate protection from infection remain unknown and no assays are currently available that document vaccination efficacy. However, vaccine formulations and delivery regimens were designed based on antibody induction and this is an area of on-going investigation.
4. The following table is provided as general guidance for test selection and interpretation:

Clinical Scenario	Spike* (IgG or Total)	Nucleocapsid (IgG or Total)
Evaluation of prior viral infection >11 days ago	Positive	Positive
Evidence of vaccination (after full course)	Positive	Negative
Evaluation of possible MIS-C **	Positive	Positive
* Includes Spike Receptor Binding Domain (RBD)		
** Multisystem Inflammatory Syndrome in Children		

**Recommendations:** Recommendations are listed above in the box at the beginning of the document.

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