Diagnostic Testing for SARS-CoV-2

Diagnosis of COVID-19 requires molecular detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR). Detection of SARS-CoV-2 viral RNA is better from nasopharyngeal specimens compared to specimens, e.g. throat, and is the preferred site. CDC also supports use of FDA authorized assays for viral testing to include those that detect SARS-CoV-2 antigen.

For initial diagnostic testing for COVID-19;

- Obtain a single nasopharyngeal (NP) swab specimen of the upper respiratory tract
- Molecular, RNA nucleic acid amplification test (NAAT) is the gold standard and should be used for identification and confirmation of COVID-19
- A nasopharyngeal (NP) specimen is the FDA-preferred sample. If this specimen is not available, as of March 23, 2020, the FDA identified the following alternatives as acceptable:
  - oropharyngeal sample collected by a healthcare professional (HCP);
  - mid-turbinate sample by onsite self-collection or HCP (using a flocked tapered swab); or
  - anterior nares sample by onsite self-collection or HCP (using a round foam swab).
Personnel should adhere to standard procedures associated with other respiratory pathogens, such as seasonal influenza and other human coronaviruses, when they transport specimens within a facility. Refer to CDC recommendations for more details on biosafety practices for specimens.3

Priorities for Laboratory Diagnostic Testing for SARS-CoV-2

Priorities for testing various populations are outlined in the algorithm titled Molecular Testing Algorithm available on the Pulse website.

Screening of Asymptomatic Populations at Higher Risk of Having or Transmitting SARS-CoV-2:

Recent experience with outbreaks in nursing homes and those in need of urgent scheduled or unscheduled care, e.g. pregnant women, emergent surgery, has identified some frequently do not report typical symptoms such as fever, cough and shortness of breath; some may not report any symptoms. Unrecognized asymptomatic and pre-symptomatic infections likely contribute to transmission in these and other healthcare settings. Therefore, screening of those not listed in the priorities listed above are increasingly important and providers are requesting testing be made available.

See Table 1 for which populations should be tested, timing, and specific method of detection should be used. The assumptions supporting recommendations in Table 1 are:

- Rapid test methods provide shorter turn around time but often are less sensitive.
- Rapid antigen test method is an acceptable method for screening for infection
- Adequate lab supplies and test kit capacity are available to meet priorities for Tier 1 or 2.
- Adequate personal protective equipment (PPE) is available at the ministry for care of PUIs/COVID-19
- As part of resuming operations, test all patients scheduled for a procedure that requires an overnight stay to allow for molecular test resulted prior to surgery performed within 2 midnights (two calendar days) prior to the procedure.

**NOTE:** Asymptomatic community members that wish to be tested should be referred to their primary care providers office, or to an available community testing provider (such as national pharmacy chains or testing clinics). They should not be sent to the emergency room for testing.
Table 1. Recommended Testing of Asymptomatic Patient Populations who are at higher risk of having and/or transmitting COVID-19 disease who present to the hospital for non-COVID-19 related services; Timing & Method

<table>
<thead>
<tr>
<th>Effective 7/21/2020*</th>
<th>Timing</th>
<th>Key Aspects</th>
<th>Key Aspects</th>
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</thead>
<tbody>
<tr>
<td><strong>Populations at higher risk of having and/or transmitting COVID-19 disease</strong></td>
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<tr>
<td><strong>When to Test</strong></td>
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<tr>
<td><strong>Rapid, molecular nucleic acid amplification test (e.g. AbbottID Now).</strong></td>
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<tr>
<td><strong>Sample:</strong> nasopharyngeal (NP) swab and test soon after collection; do not place swab into viral transport media</td>
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<tr>
<td><strong>Turn-around time (TAT) for results:</strong> 15-30 minutes, average</td>
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<tr>
<td><strong>Type:</strong> detects RNA of SARS-CoV-2</td>
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<tr>
<td><strong>Standard, molecular RT-PCR NAAT - In House, from Ministry’s Clinical Lab</strong></td>
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<tr>
<td><strong>Sample:</strong> NP Swab and then place into viral transport media following procedure from the Lab</td>
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<tr>
<td><strong>TAT for results:</strong> 4-6 hours, on average, from receipt of specimen in the Lab</td>
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<tr>
<td><strong>Type:</strong> detects RNA of SARS-CoV-2</td>
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<tr>
<td><strong>Standard, molecular RT-PCR NAAT - Send out to commercial or reference Lab</strong></td>
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<tr>
<td><strong>Sample:</strong> NP Swab then place into viral transport media following procedure from the Lab</td>
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<tr>
<td><strong>TAT for results:</strong> 3 days, on average</td>
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</tr>
<tr>
<td><strong>Type:</strong> detects RNA of SARS-CoV-2</td>
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</tbody>
</table>

| **Pregnant women - asymptomatic** |        | Use if available and urgent results needed. If not available use standard RT-PCR | x; if rapid test not available. Check with Lab on TAT related to when results may be available. |
| **Patients needing surgery - asymptomatic** |        | Use if available and urgent results needed. If not available use standard RT-PCR | x; if rapid test not available. Check with Lab on TAT related to when results may be available. |
| **Patients needing invasive procedure - asymptomatic** |        | Use if available and urgent results needed. If not available use standard RT-PCR | x; if rapid test not available. Check with Lab on TAT related to when results may be available. |
| **Patients from residential group settings - asymptomatic** | Upon arrival | (if rapid test negative or not available - order standard RT-PCR test) | x |
| **Persons from correctional or detention facilities - asymptomatic** | Upon arrival | (if rapid test negative or not available - perform standard RT-PCR test) | x |
| **Residents from Skilled Nursing Facility (SNF) and Assisted Living Facility (ALF) - asymptomatic** | Upon arrival | (if negative or not available - perform standard RT-PCR test) | x |
| **Dialysis patients - Asymptomatic** | Upon arrival | (if rapid test negative or not available - perform PCR test) | x |
| **Pre-discharge to SNF and Assisted Living - Asymptomatic** | Start 3 days prior to transfer | (if available, order as initial test. Order second test using standard RT-PCR at least 24 hrs after initial) | x; if rapid test is not available order both initial and second test 24 hrs later |
| **Asymptomatic patients from other congregate living situations** | Upon arrival | (if negative or rapid test not available - perform standard RT-PCR test) | x |

Use if RT-PCR testing is recommended and not available in-house. Check with Lab regarding TAT for results.
Repeat Testing of Patients Who've Recovered from COVID-19

There is ongoing investigation of the correlation between detection of SARS-CoV-2 RNA and period of transmissibility (infectivity) for a person with COVID-19; evidence to date indicates transmissibility is significantly reduced after acute infection. Therefore, repeat molecular testing after either 10 days following onset of symptoms or from date of initial detection of viral RNA is NOT recommended due to the likelihood that such testing only detects remnant RNA and it is unlikely that the person can transmit infection to others.

For patients meeting either of the criteria below, repeat testing is NOT recommended -

- **Symptom-based Criteria for Patient with initial symptoms of acute SARS-CoV-2**
  - At least 1 day (24 hours) has passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and,
  - At least 10 days have passed since symptoms first appeared

- **Time-based strategy for Patient with no symptoms of acute SARS-CoV-2 but tested positive**
  - 10 days have passed since the date of their first positive COVID-19 diagnostic test, assuming they have not subsequently developed symptoms since their positive test. Note, because symptoms cannot be used to gauge where these individuals are in the course of their illness, it is possible that the duration of viral shedding could be longer or shorter than 10 days after their first positive test.

Patients meeting these criteria do NOT need another molecular test prior to any subsequent outpatient procedure or inpatient surgery requiring an overnight inpatient admission. The patient should be treated as having recovered from the COVID viral infection.

Antigen Testing

Antigen tests are designed to detect proteins from the virus that causes COVID-19 in respiratory specimens, for example nasal swabs. Antigen tests are very specific for the virus but are not as sensitive as molecular tests. This means that a positive result is accurate, but a negative result does not rule out infection.

- Sensitivity = 80%, when compared to an EUA molecular device. Specificity= 100%
- Specimen can be either a nasopharyngeal (NP) and nasal (NS) swab tested either directly or after the swabs have been added to either Copan UTM or the CDC's formulation of viral transport media (VTM)
- Antigen is generally detectable in upper respiratory specimens during the acute phase of infection.

Positive antigen result - indicates that antigens from SARS-CoV-2 were detected, and the person tested is infected but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. If therapeutic or subsequent management actions are to be taken based on the positive result, providers should consider confirming the test result with a molecular test.

Negative antigen result- does not rule out COVID-19 and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient’s recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19.

**Examples of populations to screen using antigen tests:**

- Testing of residents, colleagues and clinicians in skilled nursing facilities under requirements from state-specific executive orders.
- Point of care / timely screening of persons scheduled for medically necessary outpatient procedures that require use of aerosol generating procedures (AGPs)
- Prior to initiation of immunosuppressive therapy
  - Rationale: Use of antigen test for screening conserves limited quantity of molecular test methods
Serological Antibody Test for SARS-CoV-2:

Serological tests such as serum levels of IgM and IgG antibody against SARS-CoV-2 are important for understanding the epidemiology of emerging human coronaviruses (hCoVs), including the burden and role of asymptomatic infections to be clinically useful as the supplemental tests to the nucleic acid test.\(^4\)

The following is an important perspective and caution on interpretation and use of serologic testing from the IDSA.\(^5\)

As serological testing for SARS-CoV-2 advances, there are multiple issues that need to be addressed, from test quality to interpretation. Unlike molecular tests for COVID-19 (e.g., PCR), antibody tests may be better suited for public health surveillance and vaccine development than for diagnosis. The current antibody testing landscape is varied and clinically unverified, and these tests should not be used as the sole test for diagnostic decisions. Further, until more evidence about protective immunity is available,

- serology results should not be used to make staffing decisions or
- decisions regarding the need for personal protective equipment.

Guiding Principles for Providers when Considering Serologic Testing for SARS-CoV-2:

- Person being tested understands their willingness to be tested is voluntary
- Providers ordering test are to provide consistent education to persons being tested on interpreting results – patient (test subject) education is being developed and will be on COVID-19 web
- Order testing that uses a platform (analyzer) that has demonstrated high specificity, ideally > 99%
- Goal for testing should be to improve colleague/patient health and safety and/or have operational implications
- Begin with testing groups/populations with medium or high prevalence of previous infection to minimize false positives
- Testing should be done that supports ongoing research, and understanding of value of serologic testing
- Testing can support identifying those who might donate convalescent plasma with understanding that agencies that collect plasma will repeat testing of potential donors with their method(s)

Key Populations to Consider for Serologic Testing:

- Patients and healthcare personnel (HCP), e.g. colleagues and clinicians who have recovered from confirmed COVID-19 infection
- HCP without any symptoms of COVID-19 but have or are caring for PUIs or those with COVID-19 in units or areas with high volume of patients, e.g. cohort unit, Fever and Upper Respiratory Infection (FURI) clinics, and/or Emergency Department
- Residents and colleagues in congregate living settings, especially skilled nursing and assisted living facilities, that have experienced outbreaks of COVID-19

The clinical application of serologic testing is still evolving, and the System’s Clinical Lab leadership network is actively working on getting more experience with serologic diagnostics at a select number of RHMs. Serologic assays are more retrospective and timing of development of antibody typically is after initial detection of viral RNA using NAAT. (See Figure 1) There remain uncertainties like cross reactivity of IgG antibodies with other endemic hCoVs, relationship of antibody to RT-PCR detection of viral RNA, sensitivity and specificity of serology in populations that may have high or low prevalence of infection, etc.\(^3\)
Figure 1. Sequence of Detection of SARS-CoV-2 using Laboratory Diagnostics

Note: It is uncertain how long IgG persists and if this provides protection against re-infection or long-term immunity against SARS-CoV-2

*Disclaimer: this chart is for illustrative purposes only

For illustration only: Timing of detection of RNA and antibodies likely vary by patient and method used.

Figure 2. IDSA Algorithm for SARS-CoV-2 Nucleic Acid Testing

Symptomatic Individuals***

Suspcion for COVID-19 is high
Non-Hospitalized
Lower respiratory tract symptoms
If negative, repeat testing

Suspcion for COVID-19 is low
Hospitalized
• Known exposure
• High prevalence area

Asymptomatic Individuals

• Exposed and testing is available
• Immunosuppressive procedure
• Major time-sensitive surgery
• Time-sensitive aerosol-generating procedures when PPE is limited and testing is available

Direct SARS-CoV-2 nucleic acid amplification testing

Nasopharyngeal, Nasal, or Mid-turbinate over Oropharyngeal or Saliva specimen
Provider-collected or self-collected specimens acceptable for different specimen types except nasopharyngeal

If negative, repeat testing
If negative, repeat testing (from lower tract if possible)
If negative, and high suspicion, repeat testing
If negative, do not repeat testing

***Note:
• Testing should be prioritized for symptomatic patients first.
• When resources are adequate, testing for selected asymptomatic individuals can also be considered.
References:

1. CDC. Overview of Testing for SARS-CoV-2 Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html#signs_symptoms


