General Testing Protocol Summary
Nebraska Medicine SARS-CoV-2 (COVID-19) Testing Recommendations
(Updated 04/22/2020)

Clinical Presentation: The initial symptoms of COVID-19 infection are generally mild and characterized most commonly by fever (43-98%), cough (68-82%), and shortness of breath (19-55%). In a recent report of >4700 cases in healthcare workers 92% had at least one of the symptoms of fever, cough, or shortness of breath. Other symptoms may also be present early in the illness such as headache (10-65%), myalgias (11-66%), sore throat (5-38%), loss of sense of smell or taste (up to 15%) and GI upset (nausea, vomiting, diarrhea 1-20%). Rhinorrhea (4-10%) and nasal congestion alone are relatively uncommon as opposed to many other respiratory viruses and seasonal allergies. Most persons infected with COVID-19 who are young and healthy will recover without problems. Those who are older or immunocompromised are more likely to progress to pneumonia which can be severe.

Testing Recommendations: Test availability is improving and all patients with symptoms suspicious for COVID-19 should undergo testing. Testing should be performed in patients who present with symptoms typical of COVID-19 (cough, fever, shortness of breath), those with severe symptoms, and those with a combination of the less typical symptoms listed above. Asymptomatic persons should not be tested, although there are certain situations where screening for COVID-19 may be appropriate. We recommend testing be utilized in the following way:

1. **TEST** → Hospitalized patients who have symptoms which could be compatible with COVID-19.
   - Differentiating pneumonia due to COVID-19 from other forms of pneumonia can be difficult. See information below on differentiating types of pneumonia. Other respiratory testing (respiratory panels, culture, etc.) could also be obtained if appropriate.

2. **TEST** → Those working in a healthcare environment who have symptoms which could be compatible with COVID-19. Because of their extensive and close contact with vulnerable patients in healthcare settings, even mild signs and symptoms of COVID-19 should be evaluated among potentially exposed healthcare personnel. Testing directed by Employee Health or Student Health should be performed as directed. Employee Health is open 7AM – 430PM, Monday to Friday and can be reached at 402-552-3563. After hours and weekends, call the OUCH pager (888-OUCH).

3. **TEST** → Ambulatory symptomatic patients at increased risk for poor outcomes or who work in high risk environments. This group includes:
   - Older adults (age ≥ 65 years)
   - Those who are immunocompromised or have chronic medical conditions (e.g., diabetes, chronic lung, heart, or kidney disease)
   - Long-term care facility residents or those who reside in other group settings (homeless shelter, group home, etc.)
   - Public safety workers and first responders
   - Persons performing duties or administering care in settings where spread of COVID19 would be particularly disadvantageous: group homes, prisons, assisted living facilities, long term care, etc.

4. **TESTING USUALLY RECOMMENDED** → Ambulatory symptomatic but otherwise healthy persons. With increased test availability these persons should usually be tested for COVID-19. Alternative testing such as rapid influenza testing or respiratory pathogen panels are not routinely recommended. Healthy ambulatory patients who care for those at increased risk of poor outcomes (see above) should definitely be tested.
   - Patients with respiratory symptoms who do not undergo testing should be presumed to have been infected with SARS CoV-2 and should self-isolate per available guidelines.
Directing COVID-19 Testing in Patients with Pneumonia: Differentiation of patients with COVID-19 infection from those with bacterial pneumonia can be difficult. The guidance below is provided to assist in deciding if a patient warrants COVID-19 testing. Patients with syndromes highly consistent with bacterial infection may still benefit from COVID-19 testing while those presenting with an “atypical pneumonia” with features concerning for COVID-19 should always be placed in appropriate isolation and tested.

<table>
<thead>
<tr>
<th></th>
<th>COVID-19</th>
<th>Bacterial Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Fever, Cough, Shortness of Breath, Viral prodrome (headache, myalgias, nausea/vomiting/diarrhea)</td>
<td>Fever, Cough, Shortness of Breath, Purulent sputum</td>
</tr>
<tr>
<td><strong>Lab Abnormalities</strong></td>
<td>Normal/low WBC, Lymphopenia common, Mild hepatitis</td>
<td>Leukocytosis, bandemia</td>
</tr>
<tr>
<td><strong>Procalcitonin</strong></td>
<td>Usually low</td>
<td>Elevated</td>
</tr>
<tr>
<td><strong>Exposure</strong></td>
<td>Close contact with confirmed or suspected case of COVID-19</td>
<td>None</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td>Bilateral infiltrates, “atypical pneumonia” Multifocal ground-glass opacities</td>
<td>Lobar Infiltrate</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Supportive Care Airborne, contact, droplet Isolation</td>
<td>Antibiotic Therapy Precautions per etiology</td>
</tr>
</tbody>
</table>

Testing Protocol: The decision to perform a Respiratory Pathogen Panel (RPP) should be individualized. An RPP does not need to be obtained before COVID-19 testing but may be useful in those presenting with atypical pneumonia.

- Testing will be performed using a single nasopharyngeal specimen. Oropharyngeal specimen collection is not recommended. An RPP can be run on the same swab as the COVID-19 test. Instruction on specimen collection are available on the Nebraska Now Page (https://now.nebraskamed.com/infectious-diseases-protocols/)
- Patients with pneumonia should undergo testing of sputum or of other lower respiratory tract specimens if available. Sputum induction and other aerosol generating procedures should be avoided.
- Outpatients who were tested early in their illness and then present with worsening of symptoms should be retested as false negatives have occurred early in illness.

Ordering COVID-19 Testing:

- COVID-19 testing is available in EPIC under the order COV19, see below for ordering instructions.
  - One Chart Test Name: LAB6400; COVID-19 by PCR
  - Sunquest LIS Test Name: Code is COV19, name in Sunquest is COVID 19 BY PCR
    - Alternate Test Name: Synonyms: COV19, Coronavirus, COVID19
  - One Chart Test Code: COV19
- In most cases, testing will be performed on the Roche Cobas 6800 platform. However, in certain circumstances, other samples will be tested using our laboratory developed test. In our experience, the positive and negative percent agreement between these two assays is 100%.
- Clinicians should answer any necessary questions when ordering the assay to accurately reflect their reason for testing.
- When testing is ordered on inpatients please include the associated isolation order (airborne, contact/droplet).
- When the test is ordered a flag for “COVID Rule Out” will be automatically added to the patient’s chart.
The exception to this is the pre-procedural screening (see information below) where a “COVID-19 Procedure Screening” flag will be added.

- If the test is positive an infection flag for “COVID-19” will be automatically added to the patient’s chart.

Interpreting COVID Testing Results: Two assays are currently being used to test for COVID-19. Results are slightly different between the tests and interpretation recommendations are below.

**Roche Cobas 6800 (COV19) interpretation**

- This assay is designed to detect RNA from two genes within SARS CoV 2, the E gene and the ORF1a-gene.
- If both the E- and ORF1a-genes RNA are not detected, the following will be resulted: **Not Detected - SARS CoV2 RNA NOT DETECTED by RT-PCR.**
- If both the E- and ORF1a-genes RNA are detected, or ORF1a- alone, the following will be resulted: **Detected - SARS CoV2 RNA DETECTED by RT-PCR.**
- If only the E-gene is detected, per the FDA EUA document, the following will be resulted: **Presumptive Positive – Sarbecovirus RNA DETECTED by RT-PCR.** Note that the E-gene is conserved with SARS-CoV and other coronaviruses found in bats. However, SARS CoV-1 has not been isolated since 2003 and infection from bats is highly unlikely. Thus detection of the E-gene alone should be interpreted as positive for SARS-CoV-2.
- In rare cases, the sample will fail internal controls and the result will be **Invalid.** In this situation, we suggest recollection of the sample if clinically indicated.

**Laboratory developed test (NECoV19) interpretation**

- This assay is designed to detect RNA from two genes within SARS CoV 2, the E gene and the N-gene.
- If the E-gene RNA is not detected, the following will be resulted: **Not Detected - SARS CoV2 E gene RNA NOT DETECTED by RT-PCR.**
- If the E-gene RNA is detected, the same sample will be re-tested on the next run for both the E-gene RNA plus a separate N-gene target to confirm if it is positive. If either or both the E- or N- target RNA is detected upon retesting, the following will be resulted: **Detected - SARS CoV2 E gene RNA DETECTED by RT-PCR.**
- However, if neither the E- or N-gene RNA is detected upon retesting, a result of inconclusive is reported as follows: **Inconclusive result - Please contact Microbiology director for further consultation at 402-888-5626**

How to Manage Inconclusive Results: Inconclusive result most probably reflect low levels of virus in the sample but may also represent a false positive result. We recommend the following:

- For **inpatients** who have an initial inconclusive result on a NP swab, we recommended a new respiratory tract sample be obtained 24 hours after the first sample. If possible, a lower respiratory tract specimen (sputum, tracheal aspirate, etc.) should be obtained, particularly in those with evidence of pneumonia.
  - If the new test is positive or inconclusive, the patient should be considered positive for COVID-19.
  - If the new test is negative, the need for additional testing depends on the suspicion of disease.
    - If suspicion is low, consider negative for COVID-19.
    - If suspicion is high (atypical pneumonia, high risk exposure, etc.), consider third test, again preferentially of lower tract secretions if possible.
    - Discussions with infection control are appropriate to decide if additional testing is needed in cases where results are difficult to interpret. Please contact 888-4646 to discuss.

- For **outpatients** who have an inconclusive result, a second swab should be collected 24 hours after the first swab was obtained and re-tested.
  - If the second test is negative, the patient will be considered as negative for COVID.
  - If the second test is positive, the patient will be considered positive for COVID and a public health investigation will be opened.
  - If the second test remains inconclusive, interpretation is difficult. This may indicate presence of low-level viral RNA or be falsely positive. Out of an abundance of caution, the patient should be advised to continue home isolation similar to a patient with a positive result (10 days from symptom onset and at
least 5 days of fever free without antipyretics and improving respiratory symptoms). If symptoms were to progress or worsen, obtaining additional specimens for repeat testing may be considered.

Ruling Out COVID-19:

- The currently utilized assays are very sensitive, particularly early in illness. Patients who have recently (within last 7 days) developed symptoms (either outpatient or inpatient) can usually be adequately ruled out with a single appropriately obtained NP swab. As viral levels in the nasopharynx begin to decline around a week into the illness a second test could be considered in patients who are 7 or more days into illness, especially if they have evidence of pneumonia. In these situations, a specimen from the lower respiratory tract would be preferred. Those with inconclusive results should have a second test obtained.
- Patients who were initially screened while asymptomatic (surgical screening, etc.) and subsequently develop symptoms concerning for COVID-19 should undergo repeat testing.
- Inpatients who have tested positive for COVID-19 are considered potentially infectious for 28 days from illness onset. Patients who have two negative tests at least 24 hours apart before 28 days can have the isolation flag removed and are considered not infectious. Testing to remove isolation should only be performed in those who are at least 10 days from symptom onset and who have been improving for at least 5 days (5 days of fever free without antipyretics and improving respiratory symptoms). Patients with positive tests can be discharged to home isolation. If discharged, a COVID-19 positive patient should follow the outpatient guidance on when they can exit home isolation.
- Removing patients from COVID-19 isolation should be individualized and always based on discussion with Infection Control (888-4646) and/or COVID ID physician. The Infection Control Department is ultimately responsible for removing the isolation flag.

Screening for COVID-19 in Asymptomatic Patients:

- Screening for infection in asymptomatic patients is NOT generally recommended.
- In certain high-risk situations it is acceptable such as before high risk surgical procedures or pre-bone marrow or organ transplant. (link to perioperative guidelines)
  - Pre-procedural testing should be arranged in the outpatient setting 48-72 before the procedure and be done according to currently available guidelines
  - Testing in bone marrow and organ transplant should be directed by ID experts in those areas
- Pre-operative screening in select procedures should occur within 72 hours of the planned procedure.