

LITERATURE REVIEW SARS-CoV 2 Diagnostics

By: Albert Lee, Aishwarya Kothare; Leen Azeez; Fatima Dollar; Nicholas Rowley Peer Review by: Dr. Barbara Taylor updated 9/21/2020



WHO TO TEST (CDC Recommendation)

- People with symptoms: prioritize hospitalized, live in congregate settings, healthcare workers, first responders, long term care facility (LTCF) residents, or anyone with symptoms of potential SARS-CoV 2 infection. Clinicians are encouraged to consider workup for other pathogens, as co-infections are still possible. If a positive test is found in a LTCF, serial weekly testing should be considered for outbreak control
- Asymptomatics: individuals who are prioritized by health departments or clinicians, including but not limited to: public health monitoring, sentinel surveillance, presence of underlying medical condition or disability, residency in a congregate housing setting such as a homeless shelter, residency or work in a or long term care facility, or screening of other asymptomatic individuals according to state and local plan



NUCLEIC ACID AMPLIFICATION e.g., PCR (test for active infection)

- Positive PCR may not reflect transmissible infection as reliably as positive viral culture; PCR can detect non-infectious viral fragments
- PCR sensitivity ranges from 42%-98.8% with a meta-analysis pooled sensitivity of 89%; there are patients who have reverted to positive PCR tests after already testing negative, demonstrating increased sensitivity with repeated testing
- Variables in PCR detection sensitivity include disease state, sample type and technique, and test manufacturer
- CDC recommends nasopharyngeal, oropharyngeal, nasal mid-turbinate or anterior nares swab specimen, or nasopharyngeal/nasal wash/aspirate; a specimen study suggests lower respiratory samples have higher detection rates than upper respiratory samples
- PCR detection of SARS-CoV 2 in stool samples remains positive after oral swab samples indicated convalescence, and there has been limited evidence of infectious virus recovery from stool samples, but still sparse evidence that fecal-oral transmission has played a significant role in spread*
- PCR testing has the lowest false negative rate on day 8 post-SARS-Cov 2 infection
- In patients with severe disease, infectious virus can be retrieved up to 32 days since symptom onset
- Chest CT is a good test to consider alongside PCR due to CT's higher sensitivity (97.2%) in comparison to PCR
- Pooled testing, which has been utilized by other countries, has the potential to save time, money, and increase efficiency compared to individual testing, but it starts to have diminished returns if estimated prevalence is above 10%. Many laboratories in the US report an estimated prevalence above this threshold, but this method could still be useful in small communities where prevalence is low*



ANTIGEN TESTING (test for active infection, detects viral proteins)

- Results are ready in minutes but antigen tests have lower sensitivity (~80%), a similar problem comparable to influenza
- Antigens are generally only detected when virus is actively replicating, therefore test is recommended only during acute infection, and not for asymptomatic screening.



SEROLOGY (test for past infection, detects antibodies)

- The CDC has recommended that serologic testing should not be used to establish absence or presence of SARS-Cov-2 infection
- Infectious Diseases Society of America lists three indications for serology; 1) evaluation of patients with a high clinical suspicion when RT-PCR is negative and two weeks have passed since symptom onset; 2) assessment of multisystem inflammatory syndrome in children; 3) serosurveillance studies*
- Positive serology may not confer protective immunity—there are conflicting studies on neutralizing ability of the S1 protein antibodies
- The 2003 SARS infection does not fully protect from SARS-CoV 2, and false positives due to the 2003 SARS infection are unlikely as it has not circulated the human population since 2003; positive neutralization of SARS-CoV-1 was found to be undetectable six years after infection
- IgG and IgM antibodies are observed as early as the 4th day after symptom onset. IgG has been shown to be more sensitive, but IgM was more specific and had a greater positive predictive value.
- Symptomatic patients are more likely to test positive for IgM; In acute infection, IgG levels are significantly higher in symptomatics
- Antiviral antibodies against SARS-CoV-2 have been shown to remain elevated 4 months after diagnosis*
- SARS-Cov-2 E antigen is involved in viral assembly and pathogenesis. It was demonstrated that recombinant coronaviruses lacking the E protein displayed significantly reduced viral titers and impaired viral maturation suggesting its importance during infection
- Though IgA antibodies are detected earlier, they have no clinical utility due to their low specificity
- Antiphospholipid antibodies (aPLs) have been detected in critically-ill patients; patients with aPLs have a significantly higher incidence of cerebral infarction



STATUS OF TEXAS & US TESTING?

- As of August 31th, 2020, Metro Health has reached its testing capacity goal of 8,200 tests per day, and testing capacity remains 5x higher than current need*
- In Bexar County, there have been 276, 686 COVID-19 test results to date. Incident cases have been declining as weekly positive test percentage went from 14.8% during 7/26-8/1 to 6% during 9/6-9/12*
- Many Texas health insurers and health maintenance organizations are waiving copayments, deductibles and coinsurance for COVID-19 testing; a list of participating insurance companies are listed here: <https://www.opic.texas.gov/coronavirus>
- There are currently over 60 testing sites in Bexar county with 10 of them being drive-thru testing or walk up (PCR)—they can be found here: <https://covid19.sanantonio.gov/What-YOU-Can-Do/Testing#TestingLocation>

For details and references please visit <https://oume.uthscsa.edu/longco/>

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KEY POPULATIONS

- Asians express more ACE-2 receptors on their lung parenchyma. Men express more TMPRSS2 (interact with S protein of SARS- CoV-2) than women which may also explain critical outcome differences. Male sex and age greater than 60 are significantly associated with mortality (OR 1.8 and 5.3 respectively)
- Populations experiencing homelessness are a significant source of transmission and cases, so rapid testing modalities with access to follow-up serial testing in this population may represent efficient utilization of resources
- For low socio-economic status populations, healthcare cost perception may represent a barrier to engagement in testing. These patients are more likely to present later In disease course with higher ferritin and creatinine phosphokinase levels
- Children have been reported to transmit SARS-CoV-2 past a 14 day isolation period while asymptomatic



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*Discrepancies in US Race and Ethnic Representation
in the US Population vs COVID-19 cases*

	US Population	COVID-19 Cases
Caucasian	60.4%	43.4%
Non-hispanic Black	13.4%	32.0%
Hispanic or Latino	18.3%	11.7%