RATURE REVIEW SARS-COV 2 Diagn By: Frank Jing, Albert Lee, Aishwarya Kothare; Peer Review by: Dr. Barbara Taylor



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 positive test is found in a LTCF, serial weekly testing should be considered for outbreak
- 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 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, but researchers are unable to culture from stool samples, suggesting that this may not be a route of transmission
- 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 after symptom onset
- Can consider Chest CT alongside PCR due to CT's sensitivity (97.2%) in comparison to PCR



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

- Results are ready in minutes but antigen tests have suboptimal sensitivity, also seen in influenza rapid tests
- · 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 <u>not</u> be used to establish absence or presence of SARS-Cov-2 infection
- 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 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
- 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 9th, 2020, Metro Health's testing capacity is 7, 580 per day, below the estimated need of 8.200 tests per day based on our population; this does not include unreported tests
- There have been 279,745 COVID-19 test results to date. During the week of July 21st, 13.7% of tests were positive, and 0.2% inconclusive
- 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 40 testing sites in Bexar county with four of them being drive-thru testing (PCR) by appointment -they can be found here: https://covid19.sanantonio.gov/What-YOU-Can-Do/Symptoms-Testing/Map-of-COVID-19-Testing-Sites-in-Bexar-County



KEY POPULATIONS

- Men express ACE-2 (the receptor for SARS-CoV-2 entry) more than women and may have a predilection for critical disease; 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

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%