LITERATURE REVIEW SARS-CoV 2 Diagnostics

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WHO TO TEST (CDC Recommendation update 3/18/2021)

- People with symptoms of COVID-19.
- People who have had close contact (within 6 feet for >15 minutes) with someone with confirmed COVID-19. Exceptions to this:
  - Those who have tested positive for COVID-19 in the last 3 months and remain asymptomatic.
  - Those who are fully vaccinated do not have to be tested following exposure to someone with COVID-19.
- People who take part in activities that put them at high risk because they cannot physically distance: travel, large social or mass gatherings, being in crowded or poorly ventilated settings.
- People who have been asked or referred to be tested by their health care provider, state or local health department.

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

- Positive PCR may not reflect transmissible infection as reliably as a 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 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.
- PCR testing has the lowest false negative rate on day 8 post-SARS-CoV 2 exposure for people who are asymptomatic.
- CDC recommends against repeat testing for at least 3 months after a positive test.
- Pooled testing, which has been utilized by other countries, has the potential to save time, money, and increase efficiency compared to individual testing, but may have diminished returns if prevalence is above 10%.
- Increasing testing frequency has shown to have a positive effect on cases averted over 100 days. Pooled testing has been identified as a way to increase testing frequency and efficiency while also reducing costs.
- Several combination tests that test for SARS-CoV 2, influenza A, and influenza B simultaneously have received FDA EUA such as the CDC flu SC2 Multiplex Assay and Xpert Xpress SARS-CoV-2/Flu/RSV tests.

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

- Results are ready in minutes, but antigen tests have lower sensitivity and specificity, also seen in influenza rapid tests.
- WHO recommends that if access to RT-PCR assay is limited or turnaround times are too long for clinical utility, then antigen tests with minimum sensitivity of 80% and specificity of 97% can be used if test is conducted within first 5-7 days of symptom onset.
- Concerns about some rapid antigen tests' high false positive rate has led to some questions regarding its utility, particularly in asymptomatic individuals. Those with positive tests who are asymptomatic with low suspicion of COVID-19 should have a follow up nucleic acid amplification test to confirm positivity.
- Antigen tests' efficacy for community surveillance have shown mixed results as the Abbot BinaxNOW test has shown variable sensitivity of 81.4% and 35.8%, and 53.3% in asymptomatic individuals in three separate studies, while the Soria test showed sensitivity of 41.2% in asymptomatic individuals.
- A population health survey of 65% of the population of Slovenia using antigen testing (Biosesnory Standard, RapiGEN, and Abbott) demonstrated that mass antigen testing may have a role in high prevalence areas, but is of limited utility in low risk regions.
- Rapid antigen testing devices (such as PANBIO COVID-19 Ag rapid tests) may be beneficial as a mass screening test, when RT-PCR assays are not or insufficiently available, in particular in symptomatic patients and patients with high viral loads.
- The QuickNavi™-COVID19 Ag showed high specificity and appropriate sensitivity for the detection of SARS-CoV-2 in symptomatic patients.

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.
- The Infectious Diseases Society of America lists 3 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) serosurvellance
- The most reliable EUA approved commercial testing kits include: Abbott ARCHITECT SARS-CoV-2 IgG, Roche Elecsys Anti-SARS-CoV-2 Pan-Ig, Siemens Healthcare Diagnostics Dimension EXL SARS-CoV-2 IgG (CV2G), and Siemens Healthcare Diagnositcs Dimension Vista SARS-CoV-2 IgG (COV2G).
- Positive serology may not confer protective immunity-there are conflicting studies on neutralizing ability of the S1 protein antibodies
- 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 symptomatic.
- Antiviral antibodies against SARS-CoV 2 have been shown to remain elevated approximately 5 months after diagnosis in patients with mild to moderate symptoms and up to 7 months in patient swho had severe disease.

STATUS OF TEXAS

- As of June 7th, 2021, San Antonio/Bexar County is conducting over 50,000 tests per week and the percent positivity rate is 1.2%.
- 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 90 testing sites in Bexar county with 21 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