AAP COVID-19 ECHO: Pediatric Emergency Readiness & Response
LECTURE

COVID-19 Testing and Other Updates

Presented May 15, 2020
CONFLICT OF INTEREST DISCLOSURE

• In the past 12 months, I have had the following financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial service(s):

• I do not intend to discuss any unapproved/investigative use of a commercial product/device in my presentation.

• The views presented in this didactic do not necessarily represent the views and opinions of the AAP.
DISCLAIMER

- Much of the information you will hear will be out of date within the next week or month.
CURRENT SITUATION ON AVAILABILITY OF COVID-19 TESTING AND IMPLICATIONS ON COVID-19 TRANSMISSION RATES

- Supplies of tests increasing, but testing sites limited
- Reagents, specimen collection devices, and PPE shortages limit testing
- May need to prioritize testing to high-risk groups
- Available commercial serological assays do not have titers, making it unclear how to select plasma donor
APPROVAL PROCESS FOR COVID-19 TESTS

• No COVID-19 diagnostics are FDA approved
  - Emergency Use Authorization (EUA)
    ▪ To date, more than 60 EUA issued, with many tests submitted to FDA for approval

• COVID-19 Policy for Diagnostic Tests for COVID-19
  – FDA can make available unauthorized treatments or diagnostics, based on limited data, during a public health emergency.

**TYPES OF COVID-19 TESTING**

- **Viral Culture:** current infection, shedding virus
  - Cultures are not generally available
- **RT-PCR Tests/Nucleic acid amplification tests (NAATs):** detect viral RNA (or DNA)
  - NAATs developed for SARS-CoV-2 are very specific
  - In symptomatic patients, a positive NAAT result has a very high positive predictive value (PPV)

TYPES OF COVID-19 TESTING, CONTINUED

- **Antibody Tests:** prior infection
  - May be negative early after infection
  - Unknowns: if antibody presence is protective, duration of antibody
  - Better suited for public health surveillance and vaccine development than for diagnosis
  - Predictive values (PPV) likely to be lower, given the low prevalence of prior infection to SARS CoV-2 and imperfect sensitivity and specificity

**REMEMBER...**

- **Molecular tests** (respiratory specimen-based) detect virus and can be used to directly diagnose COVID-19
  - Currently, molecular tests are the only type of tests that can be used alone to diagnose COVID-19

- **Antibody tests** (serology based) detect the immune response to the infection
  - Test cannot be used to definitively diagnose or exclude COVID-19
  - Antibody tests cannot be used alone to rule out COVID-19

FDA PROCESS: DIAGNOSTICS

- **Manually performed tests**: authorized for labs certified to perform high-complexity tests
- **Automated tests**: authorized for labs certified to perform moderate complexity tests and/or point-of-care by facilities with a CLIA Waiver
- **RT-PCR or Nucleic acid amplification tests (NAATs)**: More than 40 have EUA issuances
- **Serology**: More than 15 serology-based tests have been issued EUA

[https://www.fda.gov/media/136702/download](https://www.fda.gov/media/136702/download)
PRIORITIES FOR COVID-19 DIAGNOSTIC TESTING:
(NUCLEIC ACID OR ANTIGEN)

High Priority

• Hospitalized patients
• Healthcare facility workers, workers in congregate living settings, and first responders with symptoms
• Residents in long-term care facilities or other congregate living settings, including correctional and detention facilities and shelters, with symptoms

HTTPS://WWW.CDC.GOV/CORONAVIRUS/2019-NCOV/HCP/CLINICAL-CRITERIA.HTML
PRIORITIES FOR COVID-19 DIAGNOSTIC TESTING:
(NUCLEIC ACID OR ANTIGEN)

Persons identified by public health officials or clinicians as high priority

- Persons **with** symptoms of a possible infection with COVID-19, including: fever, cough, shortness of breath, chills, muscle pain, new loss of taste or smell, vomiting or diarrhea, and/or sore throat.
- Persons **without** symptoms who come from racial and ethnic minority groups disproportionately affected by adverse COVID-19 outcomes—currently African Americans, Hispanics and Latinos, some American Indian tribes (e.g., Navajo Nation).
- Persons **without** symptoms 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 plans.

HTTPS://WWW.CDC.GOV/CORONAVIRUS/2019-NCOV/HCP/CLINICAL-CRITERIA.HTML
**Performance Characteristics of Specimens for SARS COV-2 Active Disease/Shedding**

- IDSA panel suggests nasopharyngeal, or mid-turbinate or nasal swabs rather than oropharyngeal swabs or saliva in symptomatic individuals

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VALUE OF ANTIBODY TESTING

• Detection of PCR-negative cases, especially for late presentation, low viral load, or when lower respiratory tract sampling is not possible
• Identification of potential convalescent plasma donors
• Epidemiologic studies of disease prevalence in the community
• Verification of vaccine response once antibody correlate(s) of protection identified

TARGET ANTIGENS OF ANTIBODY

- Nucleoprotein (N protein)
- Spike protein (S protein)
- Not yet clear which antibody responses are protective or lasting

METHOD OF PICKING UP ANTIBODY RESPONSE: ELISA V. RAPID DIAGNOSTIC TEST

- Rapid development of new technologies may ameliorate some of the historic technical limitations of these tests.
- A "positive" test is exceptionally difficult to interpret because the performance of these tests is not well known. For some assays both sensitivity and specificity may be poor, or at the very least undefined.
Problem ‘pitfalls’ of serology currently (serological assays are not well-validated)

- **False negative:** too early in disease course, mild illness
- **False positive:** IgM, potential cross-reactivity with common cold coronaviruses (e.g. HKU1, NL63, OC43, 229E)

**Sensitivity:** ability to correctly identify those with disease (true positive rate); highly sensitive test $\rightarrow$ few false negative results.

**Specificity:** ability to correctly identify those without disease (true negative rate); highly specific is able to designate an individual who does not have a disease as negative. Highly specific test has few false positive results.

**Knowing the prevalence of COVID19 is important: If prevalence is low, positive predictive value is low, even using a test with high sensitivity and specificity. (To increase the positive predictive value of screening test, test only those at high risk of developing COVID19).**

Need to validate tests so as to improve the sensitivity/specificity of test.
CHALLENGES WITH RUNNING A ‘SEROLOGY’ TEST

• Labs must perform validation studies of commercial reagents

• 96-98% specificity
  – Means a positive test result is more likely a false-positive result than a true positive result if the prevalence or pretest probability is 5% or less
**Potential Problems with ‘Antibody’ Test?**

- **Cross Reactivity:** other coronaviruses, other agents
- Antibody tests are not for diagnosing active infection
  - The current tests look at IgM and IgG antibodies

*Remember: These tests may be able to let us know if someone has been infected and recovered from COVID-19*
HOME TEST KITS FOR COVID-19

• FDA is supportive of at-home testing if data and science support consumer safety and test accuracy
  – At this time, none are authorized
  – April 20, 2020, the FDA authorized the first COVID-19 test for home collection of samples to be sent to a laboratory for processing and test reporting.
    ▪ Authorization is specific only for LabCorp’s COVID-19 RT-PCR Test
    ▪ Public health value in expanding the availability of COVID-19 testing through safe home collection.
    ▪ Home collection raises several issues: safe and proper specimen collection, proper shipment, and stability of the sample during shipment

• A physician watching the collection via telemedicine may address the issue of sample collection (if the self-collection method does not raise safety concerns), but telemedicine does not address the other issues

WHAT TO DO IF POSITIVE FOR ANY COVID-19 TEST

• Understand what this might mean
  – Asymptomatic
  – Symptomatic

• Note: If you test positive or negative for COVID-19, no matter what test, you should take preventive measures to protect yourself and others
COVID-19 Testing: Summary

• These tests should not be used as the sole test for diagnostic decisions
• Current antibody testing landscape is varied and clinically unverified
• Until more evidence about protective immunity is available, serology results should not be used to make staffing decisions or decisions regarding the need for PPE.

CLINICAL SYNDROMES AND SYMPTOMS UPDATE

• Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019
  – Temporal association with COVID-19
  – Requiring hospitalization, including intensive care
  – Evidence of multisystem inflammatory syndrome:
    ▪ Fever (persistent)
    ▪ Evidence of Inflammation (laboratory values, and clinical symptoms)
    ▪ Poor function in a single organ or many organs, and
    ▪ Absence of other known infections
  – Some children have part or all of the features seen in Kawasaki Syndrome
• ‘COVID toes’ and other dermatological features

REFERENCES

• CDC: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html


• Infectious Diseases Society for America: https://www.idssociety.org/public-health/COVID-19-Resource-Center/

QUESTIONS

• Please email COVID-19@aap.org