COVID-19 Testing – from RNA and Antigens to Antibodies

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NEW YORK CITY PUBLIC HEALTH LABORATORY

• Part of the NYC Department of Health and Mental Hygiene
• Testing focused on health of the population of NYC
  - Outbreak detection and response
  - Infectious disease
  - Biothreats
  - Environmental testing
• Approx. 200 staff
Detection of VIRAL NUCLEIC ACID:
Nucleic acid amplification test (NAAT)
• Molecular test detect viral genetic material (SARS-CoV-2 RNA)
• Best test to diagnose acute infection, inform clinical evaluation and direct infection prevention and control practices
• Performed on respiratory specimens (nasopharyngeal or oropharyngeal swab, nasal swab, saliva, sputum)

Detection of VIRAL ANTIGENS:
• Detect viral proteins in patient specimens
• Diagnosis of acute infection, may be less sensitive than NAAT
• Performed on respiratory specimens (nasal swab, NP swab)

Detection of IMMUNE RESPONSE to virus:
Antibody/Serology tests
• Detect SARS-CoV-2 specific antibodies – present 1-3 weeks after infection
• Evidence of a previous infection, NOT for diagnostic purposes
• Performed on blood (serum, dried blood spot)
NAAT tests detect viral RNA
- First tests developed for SARS-CoV-2
- Based on sequence of viral genome
- Amplify virus-specific nucleic acid and detect
- May be manual or automated, low or high throughput
LABORATORY TESTING COVID-19: VIRAL NUCLEIC ACID DETECTION

• Three main steps:

• COLLECTION – shortages of collection kits: SWABS and VTM
  • Alternate devices – 3D printed swabs, saline
  • Alternate specimen types – Nasal swabs, saliva

• RNA EXTRACTION – shortages of reagents
  • Alternate platforms
  • “No-extraction” methods

• AMPLIFICATION – shortages of PCR reagents
  • Largely mitigated
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- NEW TECHNOLOGY - CRISPR
  - Sherlock CRISPR SARS-CoV-2 test
  - Upper respiratory swab specimen
  - Extract RNA, Amplify target (RT-LAMP)
  - Detection with Cas, activates CRISPR complex
  - Cleavage of reporter - DETECTION

• **Antigen test**
  • Quidel Sofia2 SARS Antigen FIA – detects nucleocapsid protein from SARS-CoV and SARS-CoV-2
  • Specimen -> reaction tube
    • Virus disrupted, nucleocapsid protein exposed
  • Apply to test cartridge
    • Protein is “captured” and detected in reader

• **Can be performed**
  • **Point-of-Care**
  • Lower sensitivity than NAAT
LABORATORY TESTING COVID-19: SEROLOGIC TESTS
• Serologic tests are intended to detect anti-SARS CoV-2 antibodies
  • Tests can be for a specific antibody type (e.g., IgG or IgM) or a combination (e.g., IgG/IgM, total)

• A **positive** result indicates the presence of antibodies that likely resulted from an infection with SARS-CoV-2
  • **Some tests may cross react with related coronavirus**

• A **negative** result is interpreted as NO previous infection, or tested too soon
  • It may take 1 to 3 weeks for antibodies to reach a detectable level following infection
  • For persons who are currently or recently infected, test for viral RNA is indicated
  • Repeat testing may be indicated in persons with recent illness
At this time, it is **NOT** known if antibodies provide protection against re-infection

- As such, a positive test should **not** be used for return-to-work decisions or relaxation of other precautions

Serology testing can be used to:

- Determine prevalence of SARS-CoV-2 infection among a population
- Identify individual patients who may be candidates to donate plasma for therapeutic purposes

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During a public health emergency, FDA can issue emergency use authorization (EUA) which expedites test review process and, if granted, allows temporary authorization for use during emergency.

CLIA (Clinical Laboratory Improvement Amendments) categorization of tests is determined after FDA authorization is granted and determines the allowable setting for tests:

- **High complexity** – difficult to perform, require quality control, quality assurance, trained personnel, proficiency testing
- **Moderate complexity** – more complex, require a lab setting, requirements for quality control, quality assurance, proficiency testing
- **Waived** – simple to perform, low risk for erroneous results, requires a Certificate of Waiver

Tests without FDA EUA default to being categorized as HIGH complexity.

Serology tests with Emergency Use Authorizations

- May be performed only in lab with EUA – 2 tests
  - Wadsworth MIA test
  - Mt. Sinai IgG ELISA

- Commercially available kits – 10 currently available
  - all must be performed in a laboratory setting

Performance data and NPV/PPV calculator:

Under Section IV.D. of the FDA Policy for Coronavirus Disease-2019 Tests, manufacturers could “validate” a test, notify FDA, and then market and distribute the test:

- NO review by FDA
- Default to HIGH complexity status
- **191 test kits listed on FDA website under this policy**
- Report must include multiple disclaimers

Manufacturers were falsely representing tests as “FDA approved” or “FDA authorized” and as “point-of-care” tests:

- Used in point of care settings – however, NOT ALLOWABLE!!!
- Performance unreviewed

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**LAboratory testing COVID-19: fDA pOlICIES and SEROLOGY TESTS**


NEW: FDA POLICY CHANGE as of May 4, 2020

- All commercial manufacturers of serology tests must submit EUA requests with validation data within 10 business days of notification to the FDA of their validation testing (or May 18) or remove the test from the market

- Specific performance thresholds for sensitivity and specificity of serology tests recommended by FDA

- Streamlined process for EUA submissions for serology tests introduced

- https://covidtestingproject.org/
• Use of testing in the coming months, as we begin to relax mitigation policies
  • Diagnosis of cases: Viral RNA, Viral Antigen testing
  • Contact tracing will be used to curb spread of SARS-CoV-2

• How serosurvey testing data will be used
  • Detection of past cases: Serology testing
  • Determine how widespread COVID-19 was in NYC
  • Provide insight into the immune response to the virus
NYC Health Department:
• Provider page: on.nyc.gov/covid19provider
• Data page: on.nyc.gov/covid19data
• Weekly webinars: Fridays, 2 PM (sign up on provider page)
• Dear Colleague COVID-19 newsletters (sign up for City Health Information subscription at: nyc.gov/health/register)
• NYC Health Alert Network (sign up at https://www1.nyc.gov/site/doh/providers/resources/health-alert-network.page)
• Provider Access Line: 866-692-3641

Other sources:
• Vital Strategies/Resolve to Save Lives: https://www.vitalstrategies.org/covid
• ASTHO: https://www.astho.org/COVID-19