BRINGING TOGETHER A FULL RANGE OF SOLUTIONS

Abbott for SARS-CoV-2 serology

May 28th, 2020
Serology tests across the spectrum of testing needs

**SEROLOGY TESTS**
- Blood tests
- Determine if someone was infected and developed antibodies
- Detect antibodies (e.g., IgM and IgG) found in blood days to weeks after symptoms appear
- Help better understand the virus and support development of treatments and vaccines

**RAPID TESTS**
- Easy to use at point of care
- 20 µl fingerstick blood sample, venous whole blood, plasma or serum
- Results: 10–20 minutes

**LAB TESTS**
- Used on instruments in hospitals and labs
- Throughput up to 100–200 tests per hour
- Time to first result 29 minutes

NOTE: Test availability varies by country.
Molecular and serology tests expand access to testing across decentralized and centralized settings

NOTE: Test availability varies by country.
Our solutions have potential to span multiple care settings

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<thead>
<tr>
<th>Location</th>
<th>Abbott RealTime m2000</th>
<th>Alinity i</th>
<th>ARCHITECT /1000SR</th>
<th>ARCHITECT /2000SR</th>
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<td>First Responders</td>
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NOTE: Test availability varies by country.
WHO case definitions

Suspect case
A. A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset;
OR
B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case (see definition of contact) in the last 14 days prior to symptom onset;
OR
C. A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

Probable case
A. A suspect case for whom testing for the COVID-19 virus is inconclusive.
OR
B. A suspect case for whom testing could not be performed for any reason.

Confirmed case

From: Global surveillance for COVID-19 caused by human infection with COVID-19 virus Interim guidance 20 March 2020

Proprietary and confidential — do not distribute
SARS-CoV-2 RNA positivity rates by sample type

SARS-CoV-2 RNA positivity by sample type

From: W. Tan et al, medRxiv preprint doi: https://doi.org/10.1101/2020.03.24.20042382
Viral and host biomarkers in SARS-CoV-2 infection

Viral detection tests

Host immune response detection tests

Time Since Infection

Incubation
Early acute phase
Late acute phase
Convalescence / Recovery

Viral RNA
Antigen
IgM
IgG
WHO diagnostic criteria for COVID-19

• Serological surveys can aid investigation of an ongoing outbreak and retrospective assessment of the attack rate or extent of an outbreak.

• In cases where NAAT assays are negative and there is a strong epidemiological link to COVID-19 infection, paired serum samples (in the acute and convalescent phase) could support diagnosis once validated serology tests are available. Serum samples can be stored for these purposes.

WHO: Laboratory testing for coronavirus disease (COVID-19) in suspected human cases – Interim guideline. March 19th, 2020
The SARS-CoV-2 IgG assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma on the ARCHITECT i System.¹

SARS-CoV-2 IgG: 2-step indirect assay²

Step 1: 18 mins
IgG in patient sample

Step 2: 4 mins
Add Trigger Reagent

Wash to remove unbound material

Light measured and used to quantitate analyte concentration

Assay components
- Magnetic microparticles coated with recombinant SARS-CoV-2 nucleocapsid antigen
- Acridinium labeled human anti-IgG

1. Abbott ARCHITECT SARS-CoV-2 IgG Instructions for Use.
2. Data on file at Abbott Diagnostics
Positivity for IgM and IgG antibodies to SARS-CoV-2 in 67 patients

RNA+: 41.2%
RNA+: 19.2%

Data from: W. Tan et al, medRxiv preprint doi: https://doi.org/10.1101/2020.03.24.20042382

Proprietary and confidential — do not distribute
Trends in the detection of SARS-CoV-2 IgM & IgG

Positivity rates for IgM and IgG antibodies to SARS-CoV-2 in 285 patients with COVID-19 Blue=IgM; Red=IgG; Green= IgM and/or IgG

Modified from: Q-X. Long et al, Nat Medicine 2020; https://doi.org/10.1038/s41591-020-0897-1
Detection of SARS-CoV-2 antibodies to N or S antigens


ADD-00071128
SARS-CoV-2 IgG positivity – NP vs. RBD

SARS-CoV-2 IgG positivity – NP vs. RBD


Proprietary and confidential — do not distribute
ARCHITECT SARS-CoV-2 IgG – positive agreement

Data from ARCHITECT SARS-CoV-2 IgG package insert
ARCHITECT SARS-CoV-2 IgG positivity compared to PCR positivity (blue) and days after onset (red)

From: A. Bryan et al, medRxiv preprint doi: https://doi.org/10.1101/2020.04.27.20082362
ARCHITECT SARS-CoV-2 IgG – specificity and negative agreement

Data from ARCHITECT SARS-CoV-2 package insert
Specificity on 1,020 pre-COVID specimens

From: A. Bryan et al, medRxiv preprint doi: https://doi.org/10.1101/2020.04.27.20082362
The importance of being specific

• No ‘confirmation’ available for any SARS-CoV-2 serological assay
• The positive predictive value (PPV) depends on the specificity and the prevalence; the lower the latter, the lower the PPV

• Example: 100,000 individuals, 3% prevalence
  – Assay with 95% specificity: 3,000 true positives, 4,850 false positives \( \text{PPV} = 38.2\% \) (2 FP for each TP)
  – Assay with 99% specificity: 3,000 true positives, 970 false positives, \( \text{PPV} = 75.6\% \) (1 FP for each 3 TP)
  – Assay with 99.5% specificity: 3,000 true positives, 485 false positives, \( \text{PPV} = 86.1\% \) (1 FP for each 6 TP)

• Population prevalence 1.79%, specificity 99.9\%, \( \text{PPV} 94.7\% \)

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1- Data from: A. Bryan et al, J Clin Microbiol2020 aop ; PPV extrapolated from the prevalence and specificity data
ARCHITECT SARS-CoV-2 IgG – serial bleeds

Days after onset

Data from ARCHITECT SARS-CoV-2 Instruction for use

ADD-00070983
ARCHITECT SARS-CoV-2 IgG - precision

From: (1) -ARCHITECT SARS-CoV-IgG Instruction for use, (2) modified from A. Bryan et al, J Clin Microbiol2020 aop; (3)-M.S. Tang et al, Clin Chem 2020 aop
Key statements from a recent paper

• Both serial viral load monitoring and antibody response should be considered when making decisions about infection control measures, because viral load seemed to be related inversely to serum antibody response in this study.

• Serological diagnosis is important for patients who present late with a very low viral load, below the detection limit of RT-PCR assays.

• Serum IgG amounts can rise at the same time or earlier than those of IgM against SARS-CoV-2.

• The correlation between microneutralization assay titres and anti-NP IgG ($R^2=0.99$) or anti-RBD IgG ($R^2=0.96$) was better than those between microneutralization assay titres and anti-NP IgM ($R^2=0.88$) or anti-RBD IgM ($R^2=0.87$).

Correlation between Elisa ratios and PRNT

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<th>Test, virus</th>
<th>Correlations</th>
<th>S1</th>
<th>N</th>
<th>RBD</th>
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<td>PRNT\textsubscript{50}, SARS-CoV-2</td>
<td>Spearman p value</td>
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<td>2-tailed p value</td>
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*From: N.M.A. Okba et al, EmergInfDis2020 aop*
Antibody levels & neutralizing activity

Combination of SARS-CoV-2 diagnostic results

**TEST RESULTS**

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**GENERAL INTERPRETATION**

*General representation, not based on actual kit performance.

**Test results must be considered with other clinical data available to the clinician.
Testing in the context of COVID-19 disease
