COVID-19: KEEPING UP WITH A MOVING TARGET
October 21, 2020 UPDATE

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Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials, including a monoclonal antibody cocktail, dexamethasone, and several vaccine platforms.

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CME Information

To attest for CME/CE/AAPA credit, please visit

COVID19.dkbmed.com

Learning Objectives

- Discuss limitations of current testing
- Describe the difference between molecular tests and antigen tests

Thank You

This activity is supported by an educational grant from Pfizer, Inc. and in-kind support by DKBmed, LLC.

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Please see **COVID19.DKBmed.com** for additional resources and educational activities

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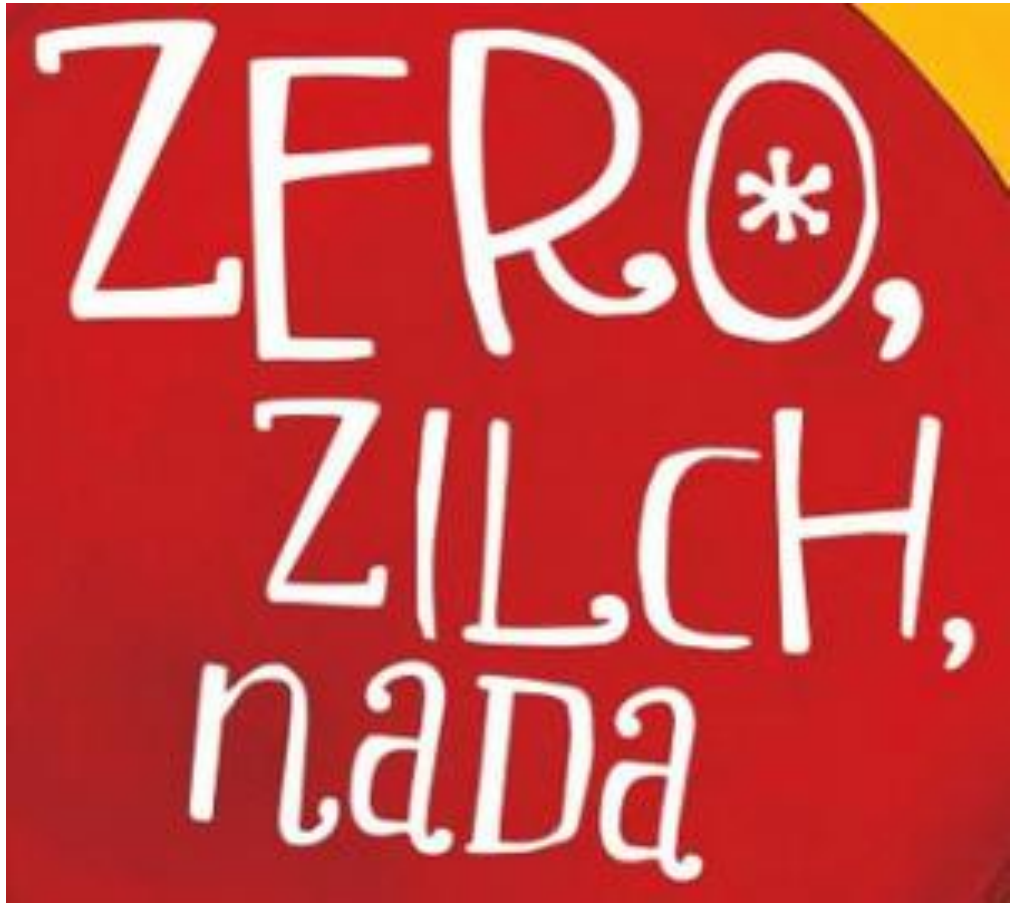
SARS-CoV-2 Testing

9 months in, still many questions

Comprehensive Assessments of Approved Testing

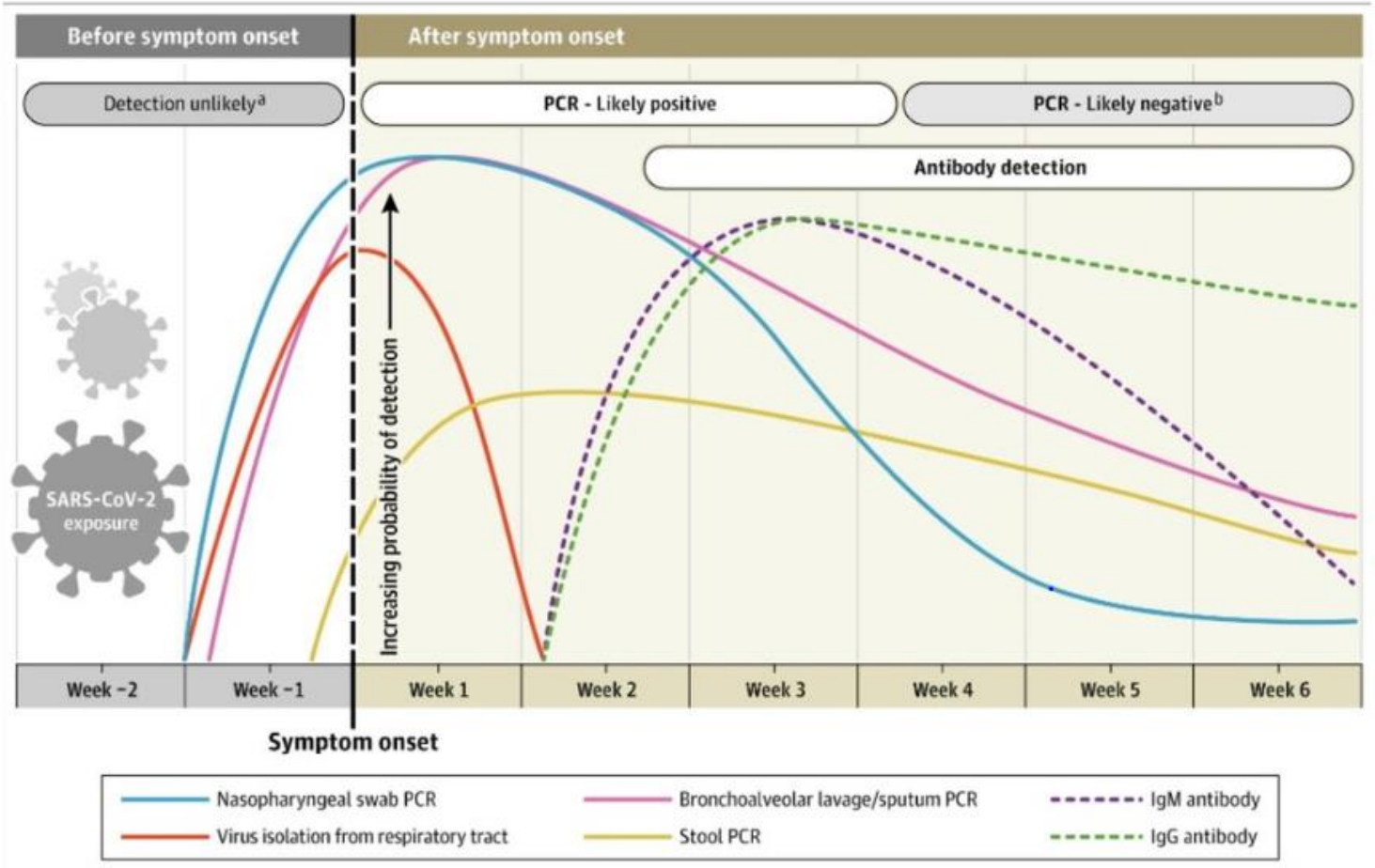


Limitations of Approved Testing

- Conditional approval (EUA):
  - Analytical validity
  - Small sample size
  - Samples from symptomatic COVID-19 hospitalized patients (higher titer)
  - No large clinical validation
  - No gold standard/benchmark
    - Molecular testing best, but unclear what is the standard
    - CT values vary among platforms

Sensitivity

Test Sensitivity Varies With Time Since Symptom Onset

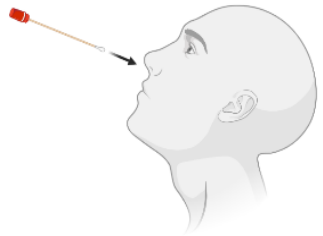


RT-PCR

COVID-19 Diagnostic Test through RT-PCR

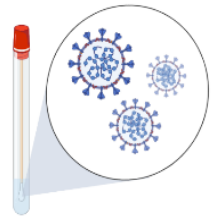
1 Nasopharyngeal swab <15 min

Cotton swab is inserted into nostril to absorb secretions.



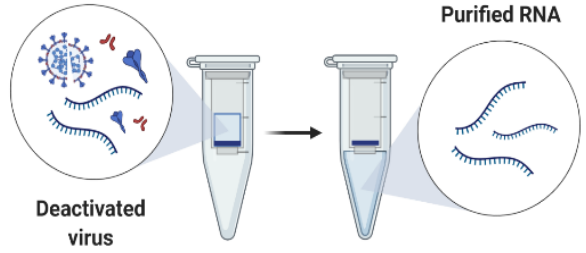
2 Collected specimen 0-72 h

Specimen is stored at 2-8°C for up to 72 hours or proceed to RNA extraction.



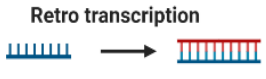
3 RNA extraction ~45 min

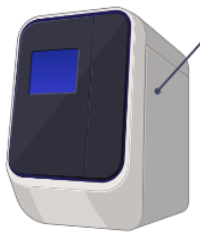
Purified RNA is extracted from deactivated virus.

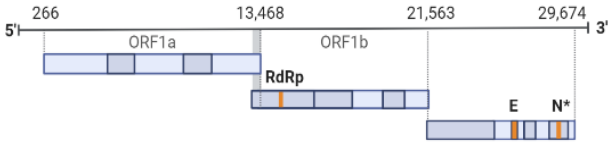


4 RT-qPCR ~1 h per primer set

Purified RNA is reverse transcribed to cDNA and amplified by qPCR.







Primers and probes for screening

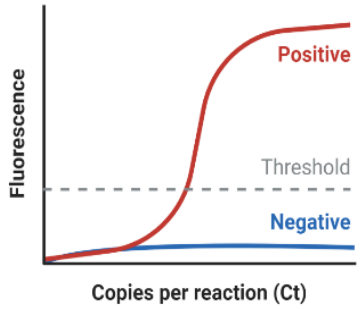
E gene First-line screening tool
- **E_Forward:** ACAGGTACGTTAATAGTTAATAGCGT
- **E_Probe1:** FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ
- **E_Reverse:** ATATTGCAGCAGTACGCACACA

RdRp gene Confirmatory testing
- **RdRp_Forward:** GTGARATGGTCATGTGTGGCGG
- **RdRp_Probe1:** FAM-CCAGGTGGWACRTCATCMGGTGATGC-BBQ
- **RdRp_Probe2:** FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ
- **RdRp_Reverse:** CARATGTTAAASACACTATTAGCATA

* N gene testing is not further used because it is slightly less sensitive.

5 Test results real-time

Positive SARS-CoV2 patients cross the threshold line within 40.00 cycles (< 40.00 Ct).



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PCR Turkey Talk

- False negatives: range 2-37%
  - Depends on stage of illness, technique acquiring sample
  - May need to repeat test if clinically suspicious

- Pooled testing: may reduce costs by batching
  - Positive pool = all in that pool need individual testing—delay.
  - Not widely used
  - Most useful if community rates are declining and low

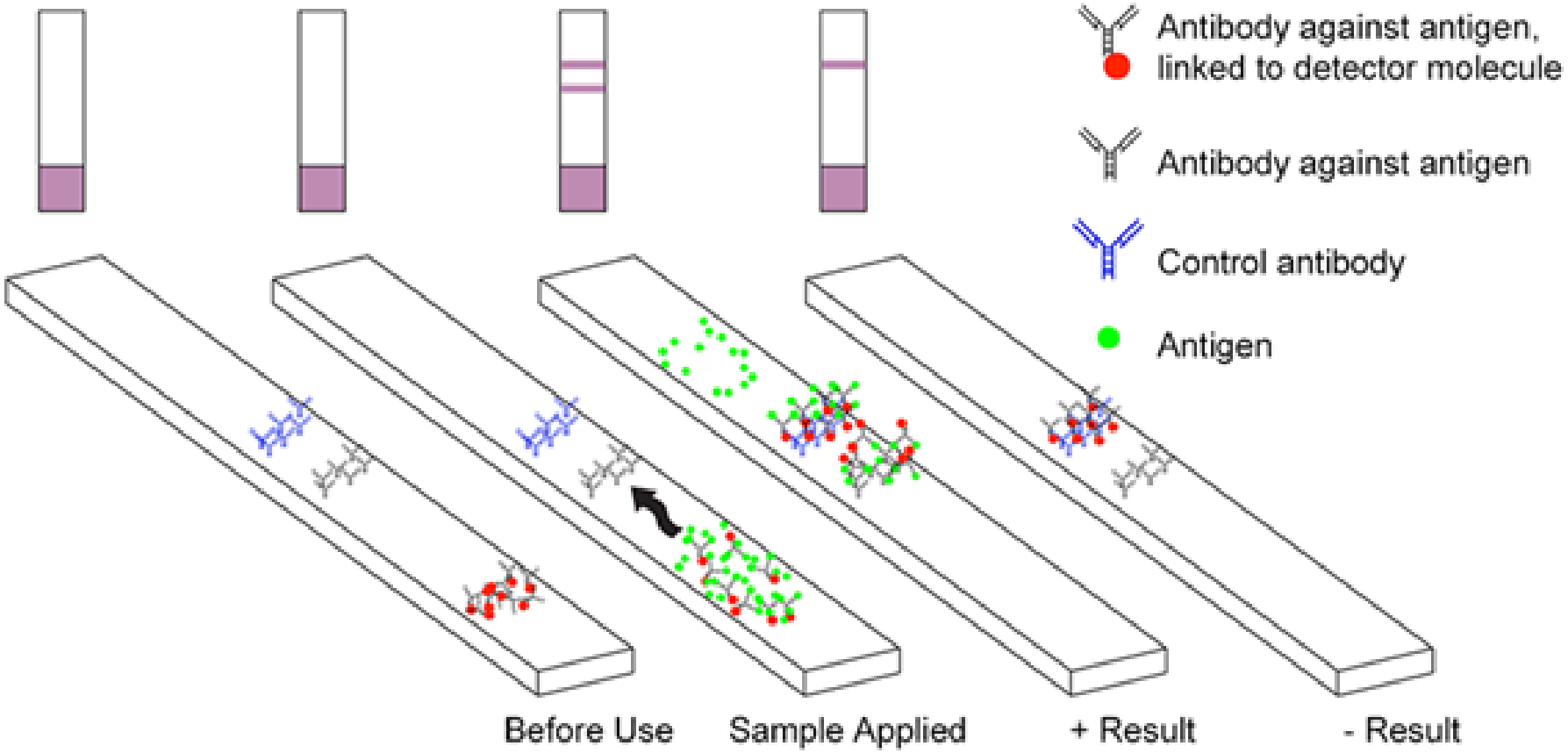
Saliva-Based Tests: Is Drool Good?

- Emerging
- Likely less sensitive than nasopharyngeal swab
  - Detects only ~ 90%
- No tests widely available
- Decreases barrier to testing
  - Who is most contagious?

A woman spits into a tube so that her saliva can be tested for the presence of the novel coronavirus. UNIVERSITY OF ILLINOIS, URBANA-CHAMPAIGN

Service RF, Science, 2020

Antigen Testing



Adapted from: Ian M. Campell, https://commons.wikimedia.org/wiki/File:Diagnostic_Medical_Dipstick.png

Rapid Testing

COVID-19 Molecular v. Antigen

Table 2. Summary of Some Differences between RT-PCR Tests and Antigen Tests

	RT-PCR Tests	Antigen Tests
Intended Use	Detect current infection	Detect current infection
Analyte Detected	Viral RNA	Viral Antigens
Specimen Type(s)	Nasal Swab, Sputum, Saliva	Nasal Swab
Sensitivity	High	Moderate
Specificity	High	High
Test Complexity	Varies	Relatively easy to use
Authorized for Use at the Point-of-Care	Most devices are not, some devices are	Yes
Turnaround Time	Ranges from 15 minutes to >2 days	Approximately 15 minutes
Cost/Test	Moderate	Low

CDC
(accessed 9/12/20)

Can the Role of Antigen Tests be Widened?

- Date: Mon 19 Oct 2020 17:01
  From: Salerno, Reynolds (CDC/DDPHSS/CSELS/DLS) <[redacted]@cdc.gov>

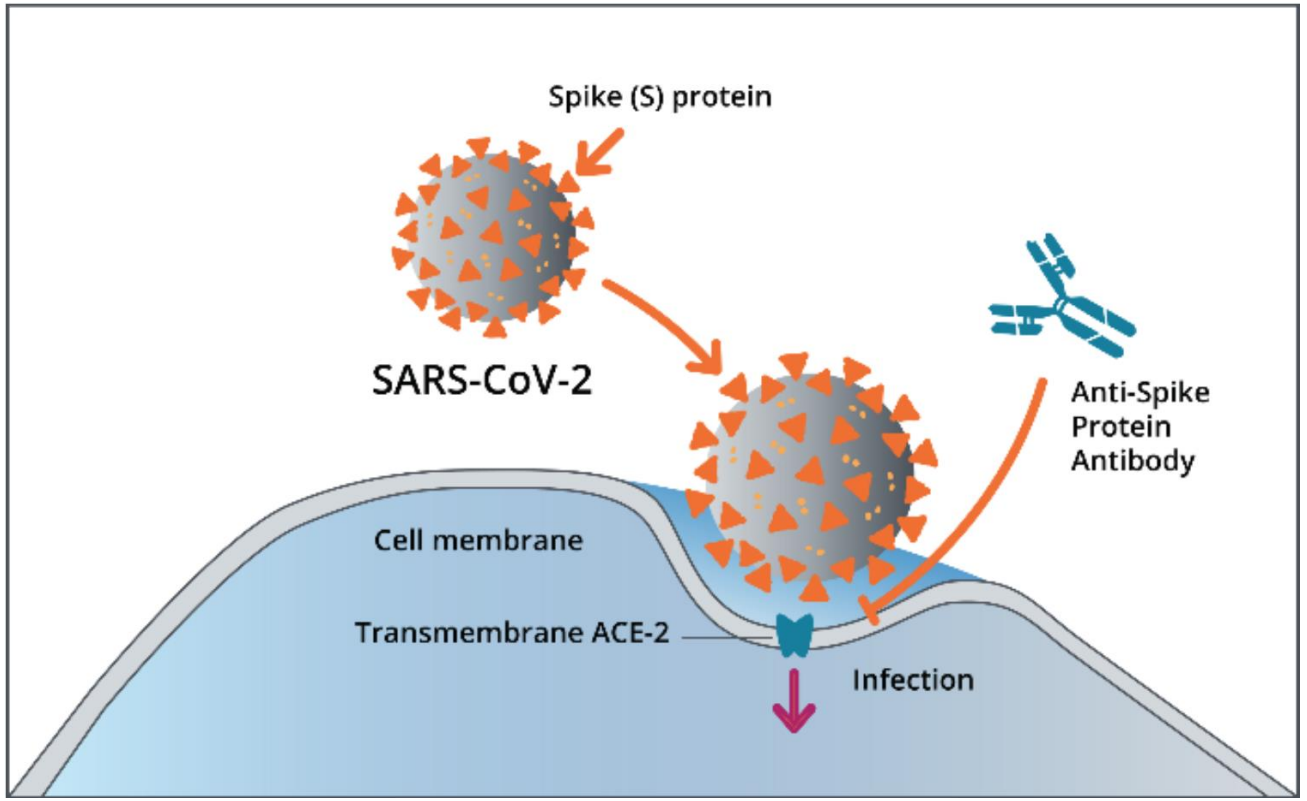
  We are working on a number of studies with different partners to evaluate the performance of all of the widely available antigen tests on asymptomatic persons. The FDA authorizations for these tests are limited to their use on symptomatic persons. We will share data as soon as we are able.

  Ren Salerno
  CDC
  Atlanta, GA (POSTED TO EIN NETWORK)

- Uncertain
- Tests hard to obtain (most purchased by the government)
- FDA EUA: only for symptomatic patients
- Low sensitivity
  - If repeated, increased false positive tests
  - Asymptomatic screening—likely with lower sensitivity as pretest probability lower.

SARS-CoV-Antibody Testing (Available Versions)

- A positive test may reflect exposure to other coronaviruses
- A positive test should not be taken as evidence of immunity
- A positive test does not mean a COVID-19 diagnosis



Testing FAQs

Q: I am a close contact, tested negative = Can I get out of jail?

A: No, incubation 2-14 d, average 5-6 to symptom onset.

Q: I have had COVID-19, I don't need to be tested?

A: Perhaps. However, many states requiring testing for entry without quarantine. There is yet no test for protective immunity.

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To ask your own question, email: QA@dkbmed.com