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IDFA Membership Briefing

COVID-19: What's the Story on Testing?

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Briefing Overview

Tom Wojno – SVP, Innovation & Member Advancement

- All lines are placed on mute during this briefing.
- Questions can be submitted via Chat throughout the briefing. Any unanswered questions will be addressed individually after the briefing.
- Only IDFA staff can view Chat questions and will answer questions without revealing their source.
- This Membership Briefing is being recorded. The recording will be available at www.idfa.org, in the Knowledge Center, on the Webinars tab.
- For technical difficulties during the briefing, send a message through the Chat box or e-mail membership@idfa.org.

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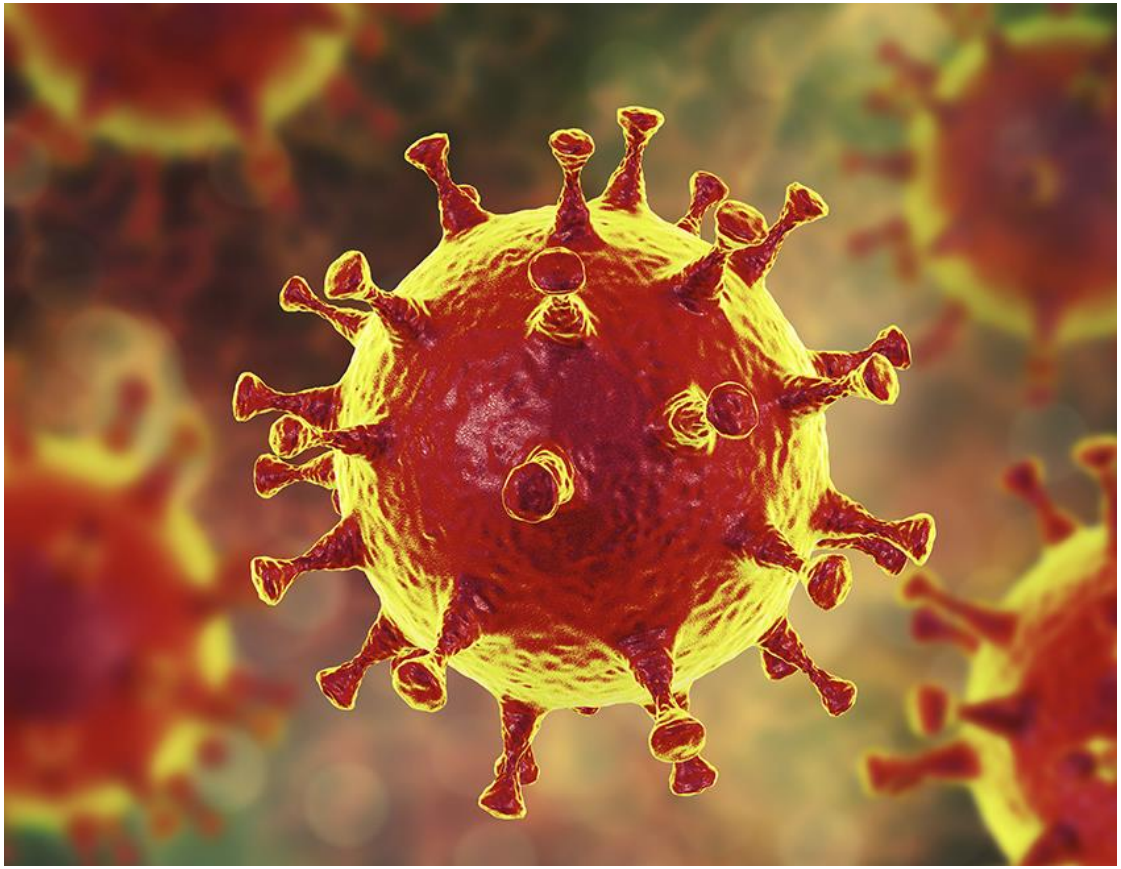
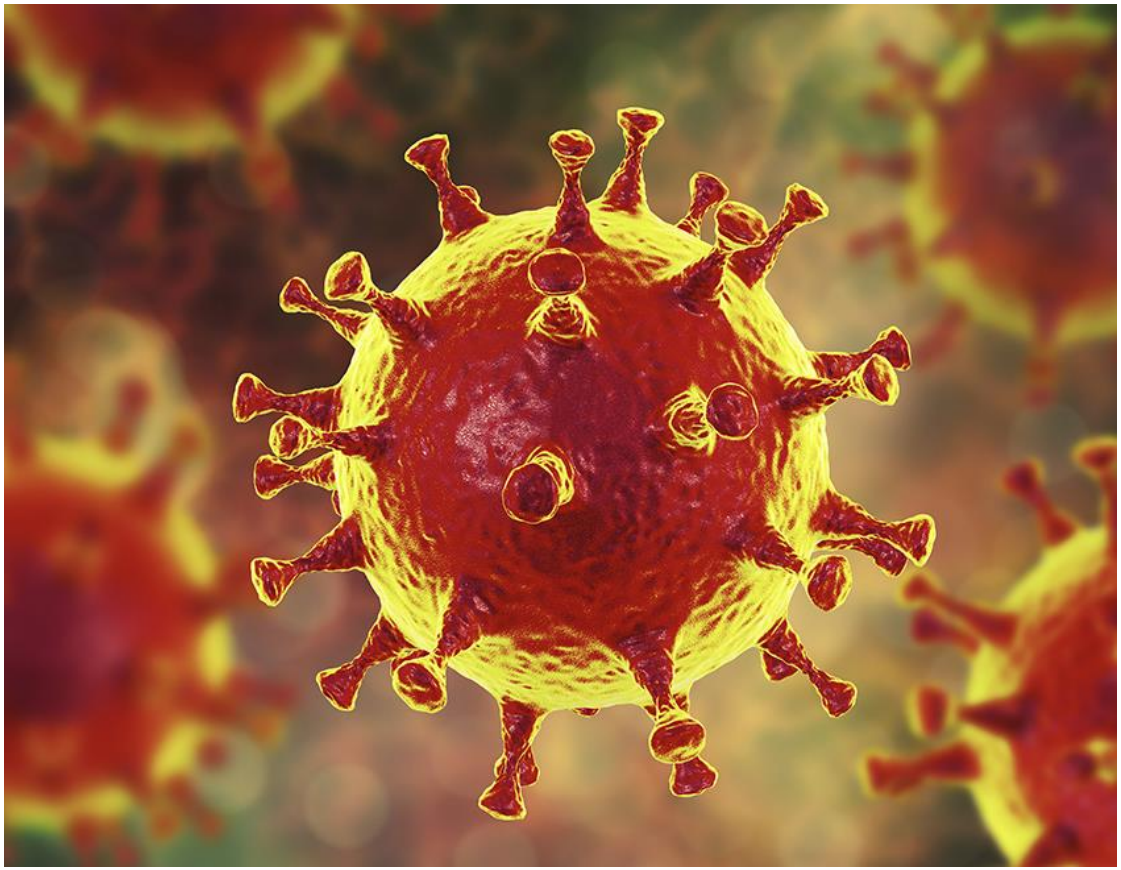
Welcome & Introduction

Joe Scimeca – SVP, Regulatory & Scientific Affairs



COVID-19: What's the Story on Testing?

S Ostroff, MD
April 29, 2020

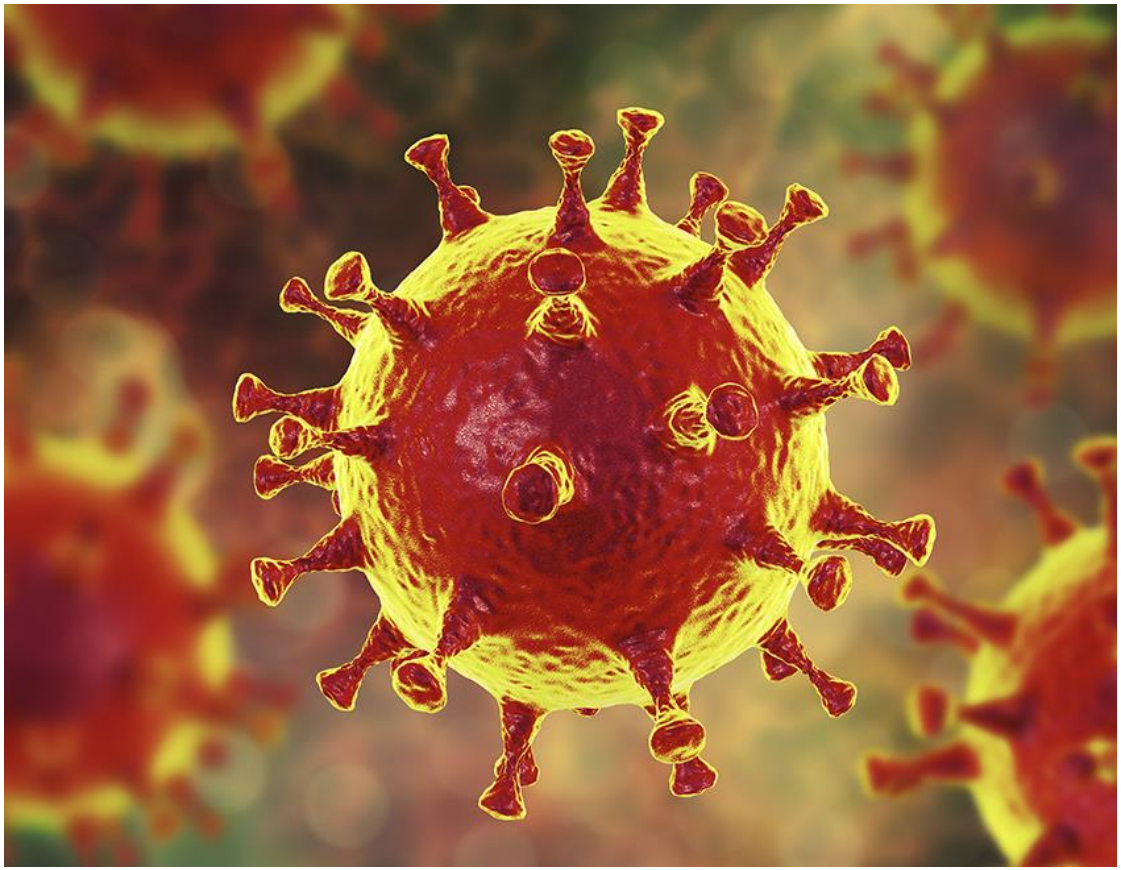


COVID-19: What's the Story on Testing?

Laboratory testing is essential for:

- Public health tracking
  - Including trends & risk factors
- Diagnosis & patient management
- Contact tracing & management
- Policy decisions on containment and mitigation efforts

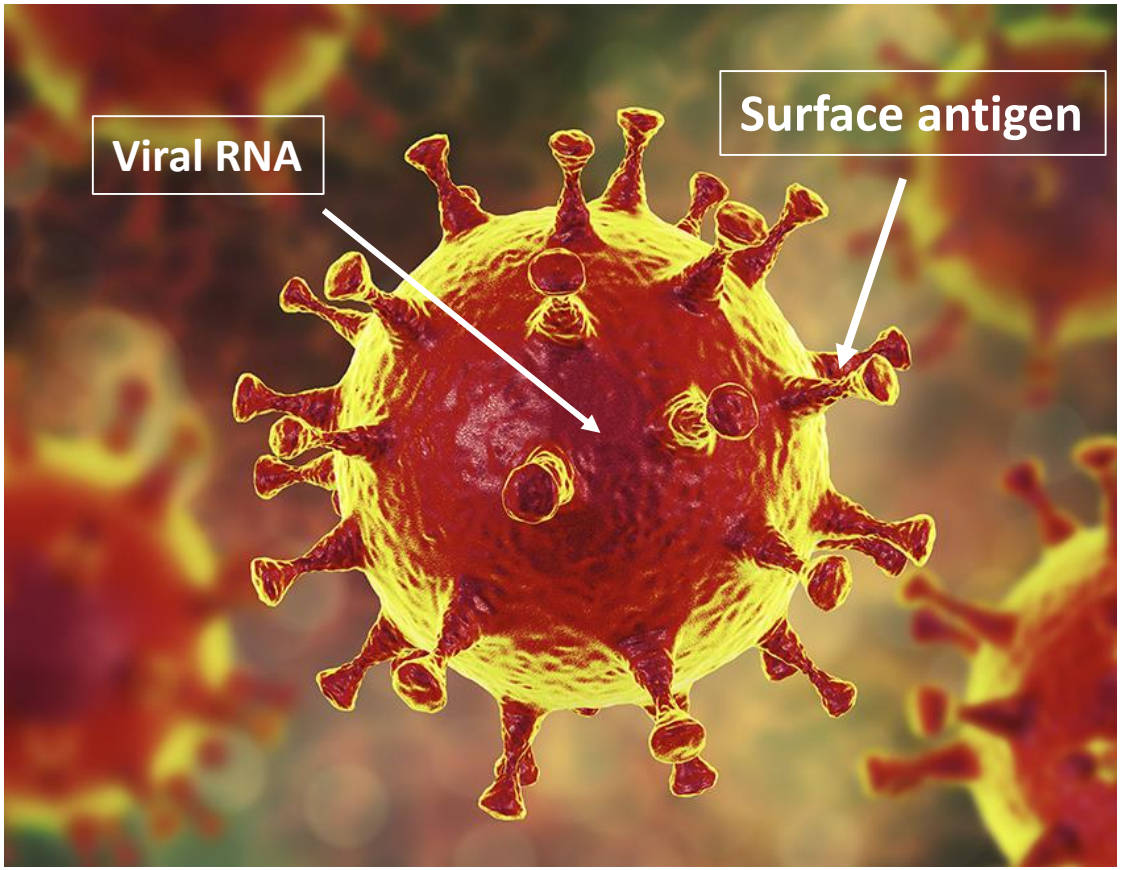
Lab testing has posed problems since COVID-19 emerged in January



COVID-19: What's the Story on Testing?

There are <u>only</u> two disease testing strategies:

- **Testing for acute infection (e.g. looking for the presence of the virus)**
- **Testing for evidence of past infection**



Testing for Acute Infection

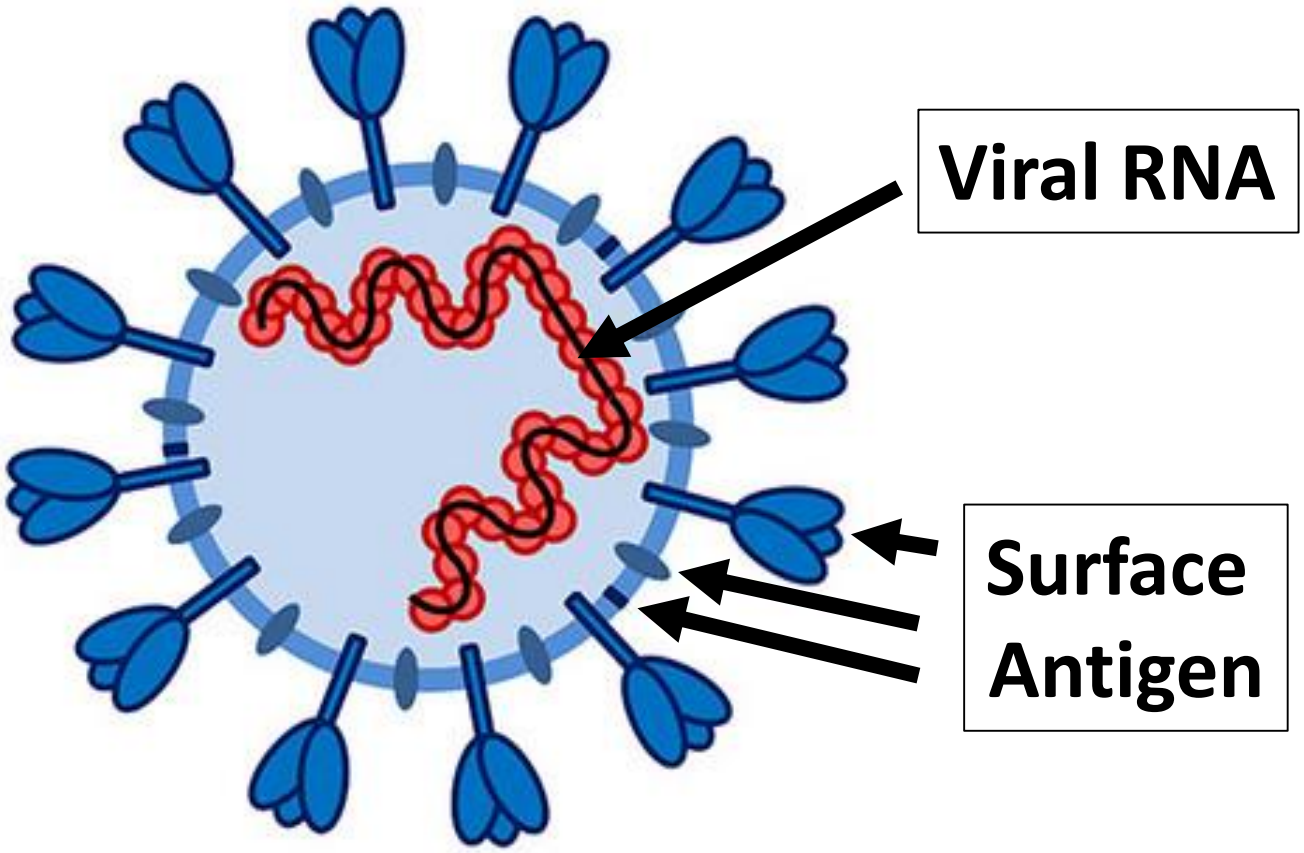
Three options

- Grow the virus in cell culture
- Identify the genetic material (RNA)
  - Polymerase chain reaction
- Capture surface antigen

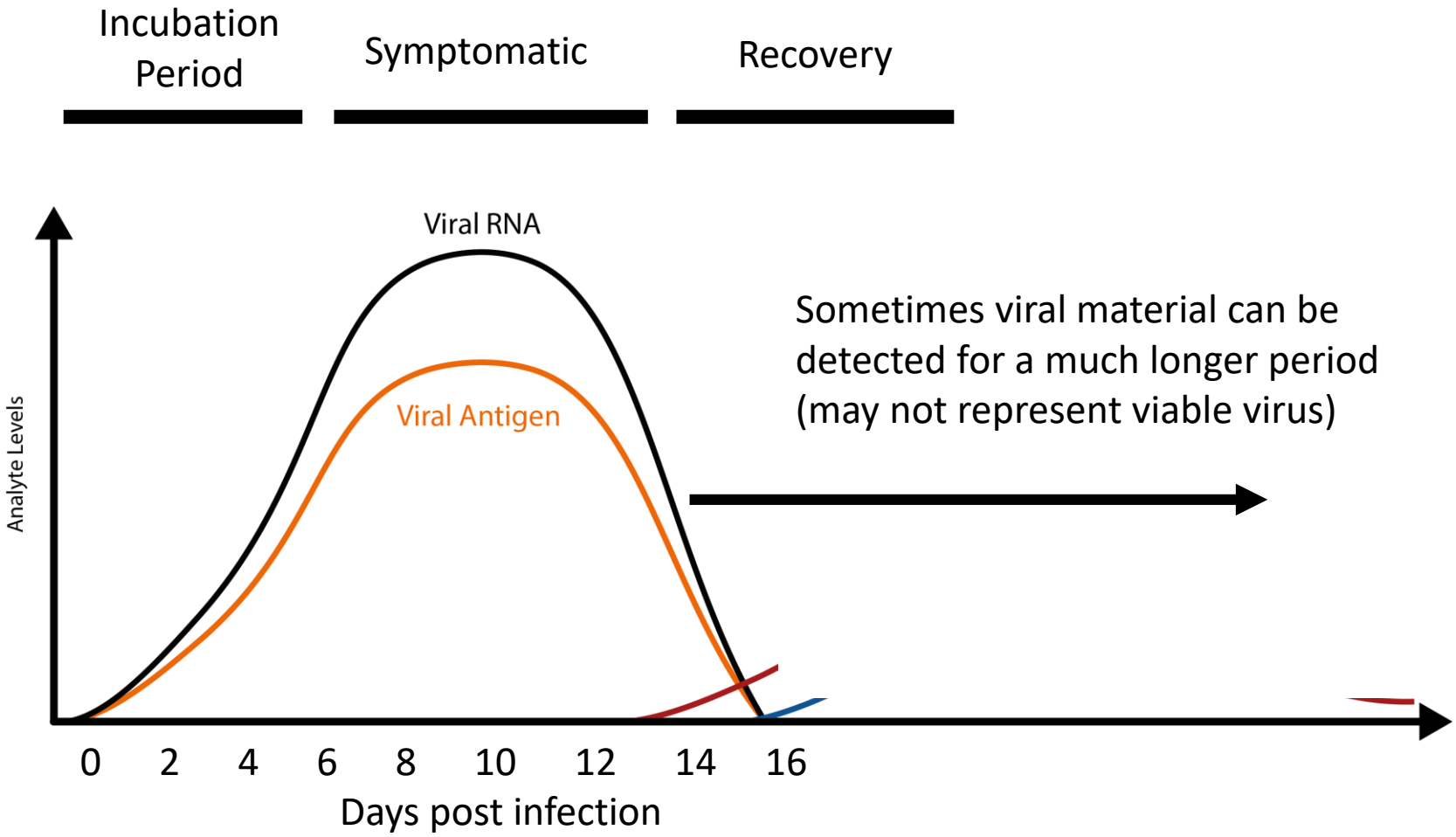
Specimen source

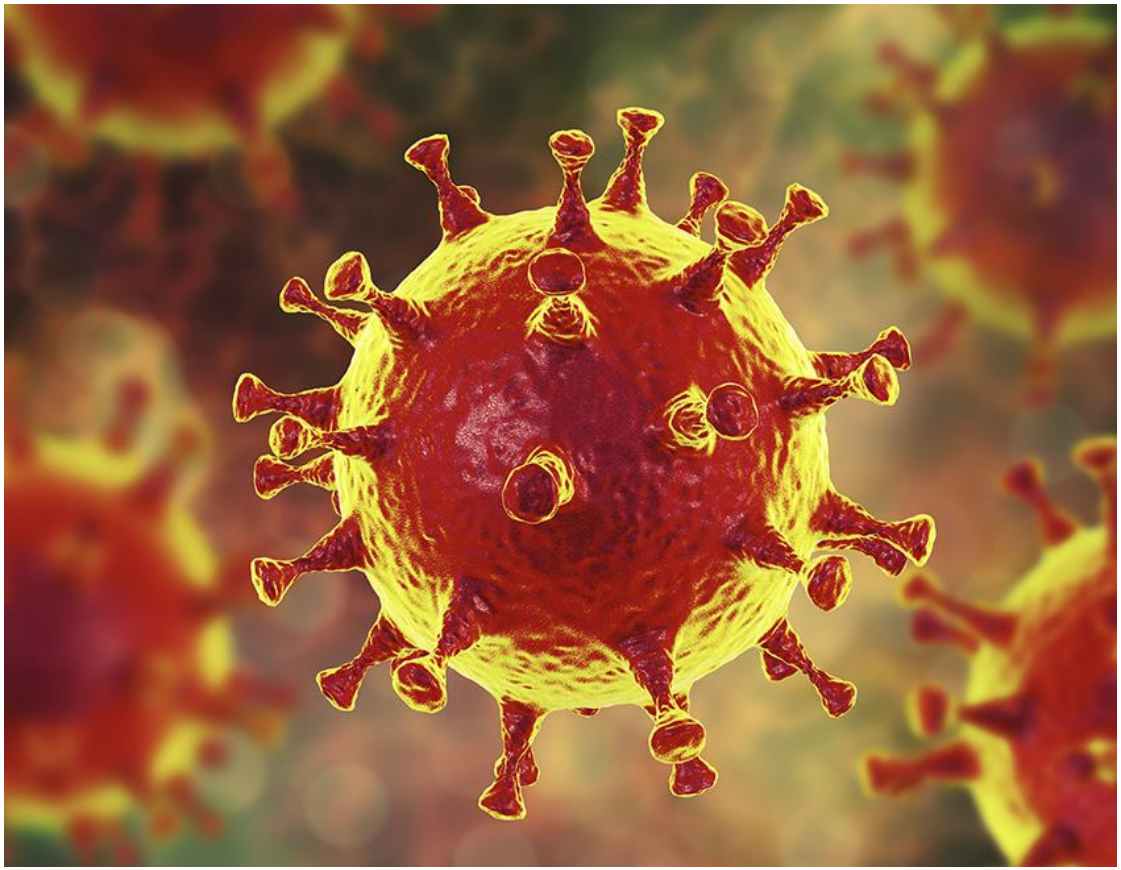
- Nasopharyngeal (NP) swab
- Nasal swab
- Oropharyngeal (OP) swab
- Saliva
- GI tract

SARS-CoV-2



Typical COVID-19 Infection

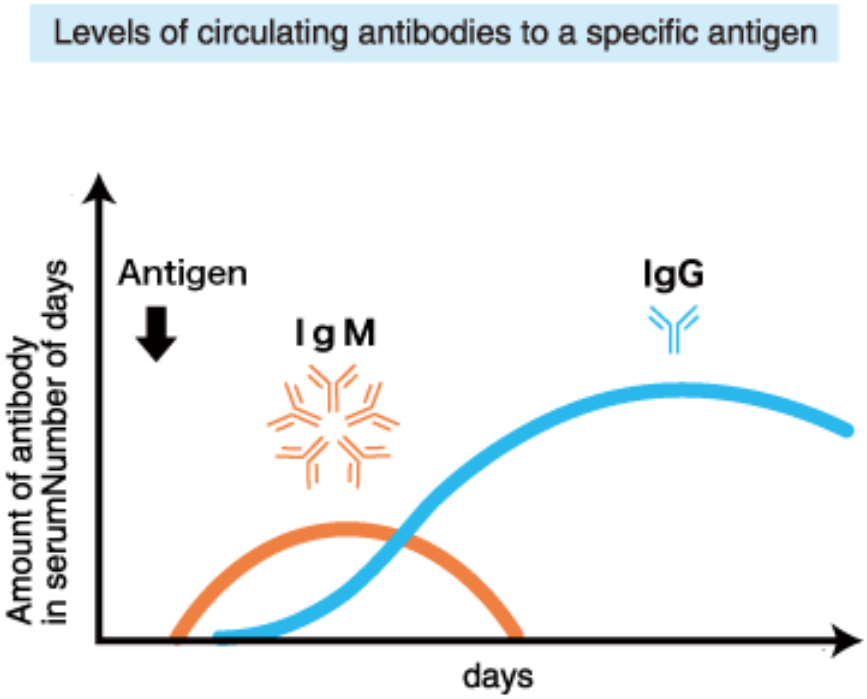




Testing for Acute Infection

- Only viral culture can tell if viable (infectious) virus is present
- PCR and antigen capture cannot
- PCR positive as long as genetic material is present
- Can identify asymptomatic, presymptomatic and ill individuals
- Can detect post-recovery
- Factors in test performance:
  - Test quality
  - Specimen quality
  - Specimen transport and storage

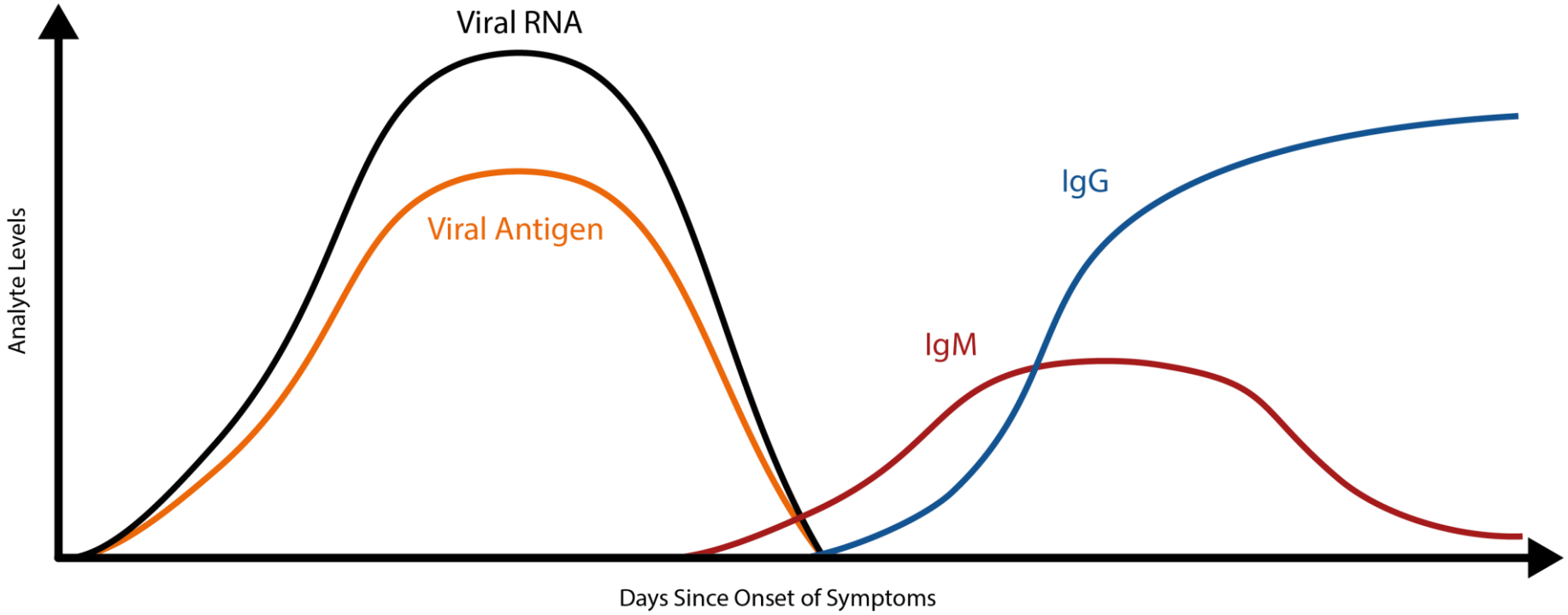
Typical Antibody Response to An Acute Infection

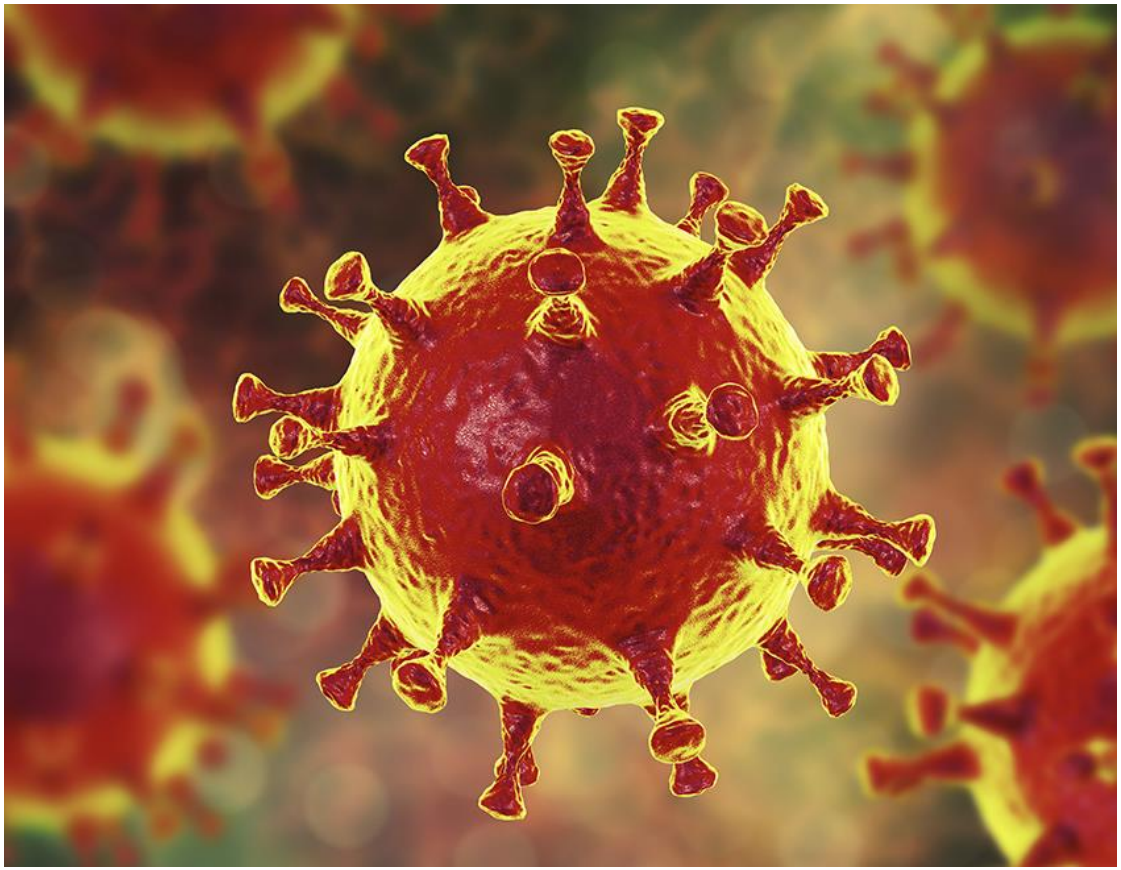


IgM antibodies: acute phase

IgG antibodies: long term memory

Typical COVID-19 Infection

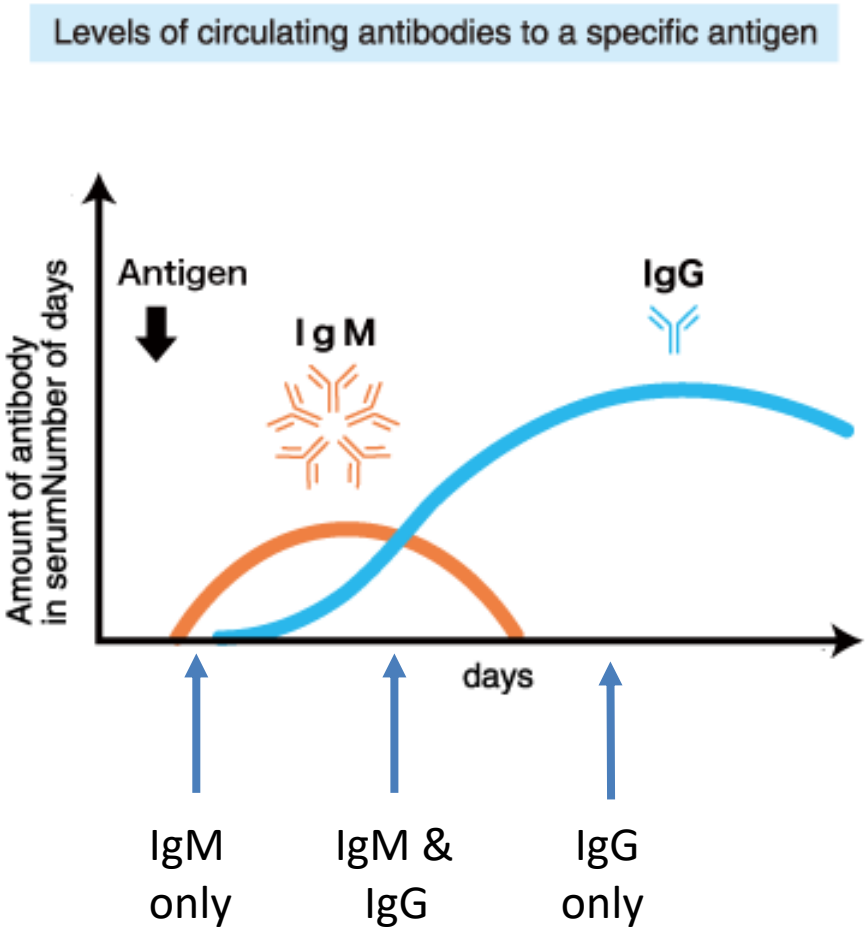




COVID-19 Antibody Response

- Antibodies produced by B lymphocytes
  - Circulate in the blood
  - Must collect blood sample to detect
- Some tests require venous blood sample
- Some fingerpick
- Most assays test for IgM and IgG
- Tests can be qualitative (present/absent) or quantitative (antibody titers)

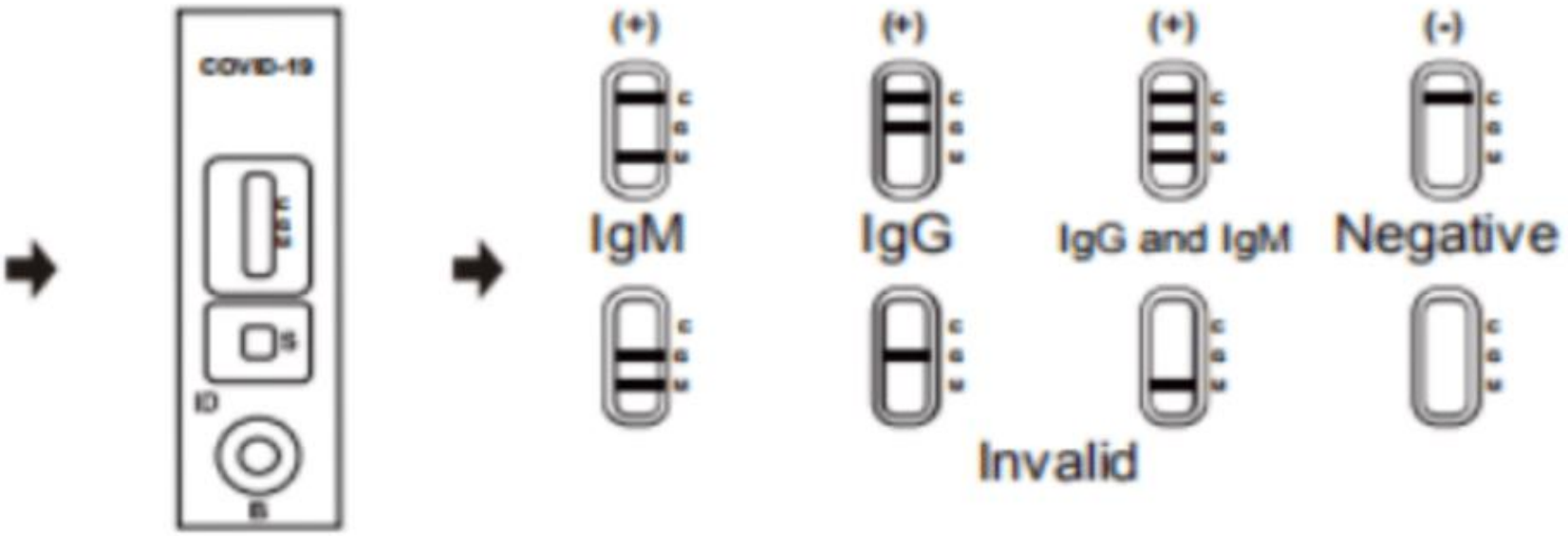
Typical Antibody Response to Any Acute Infection

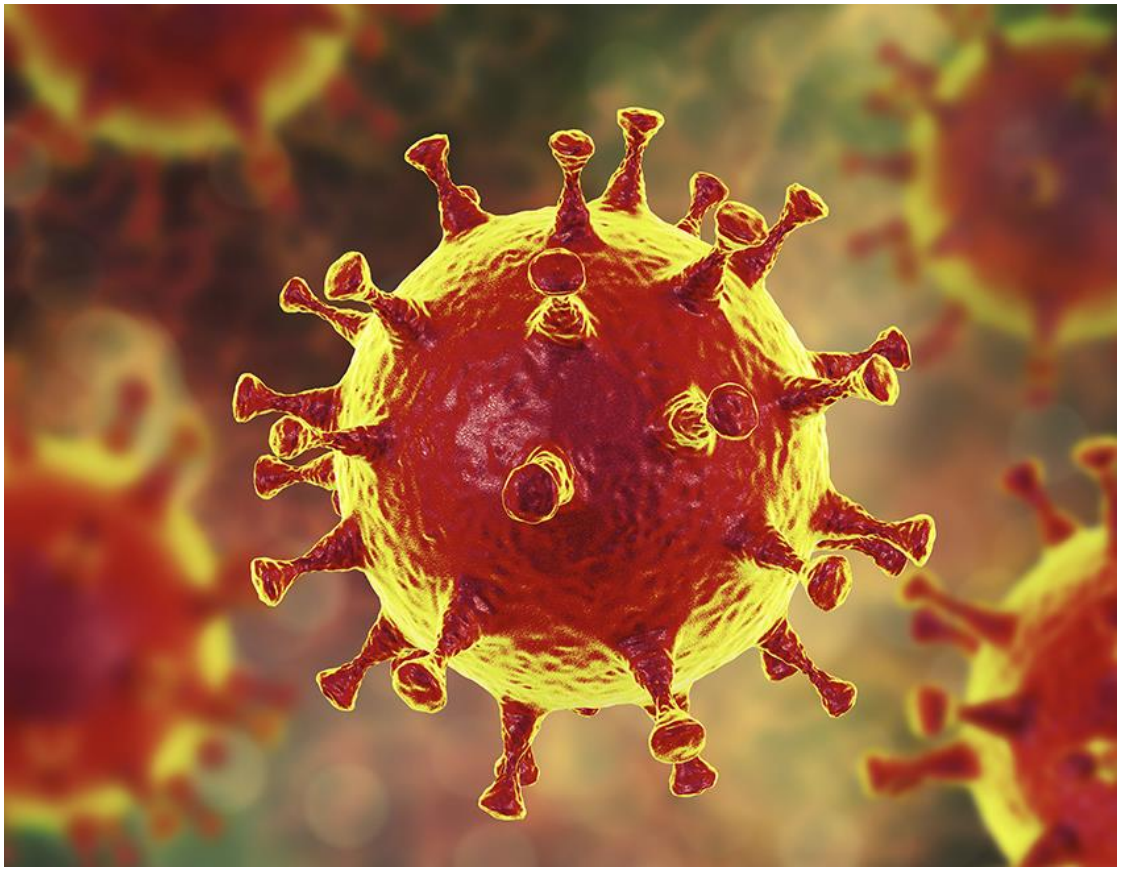


IgM antibodies: acute phase

IgG antibodies: long term memory

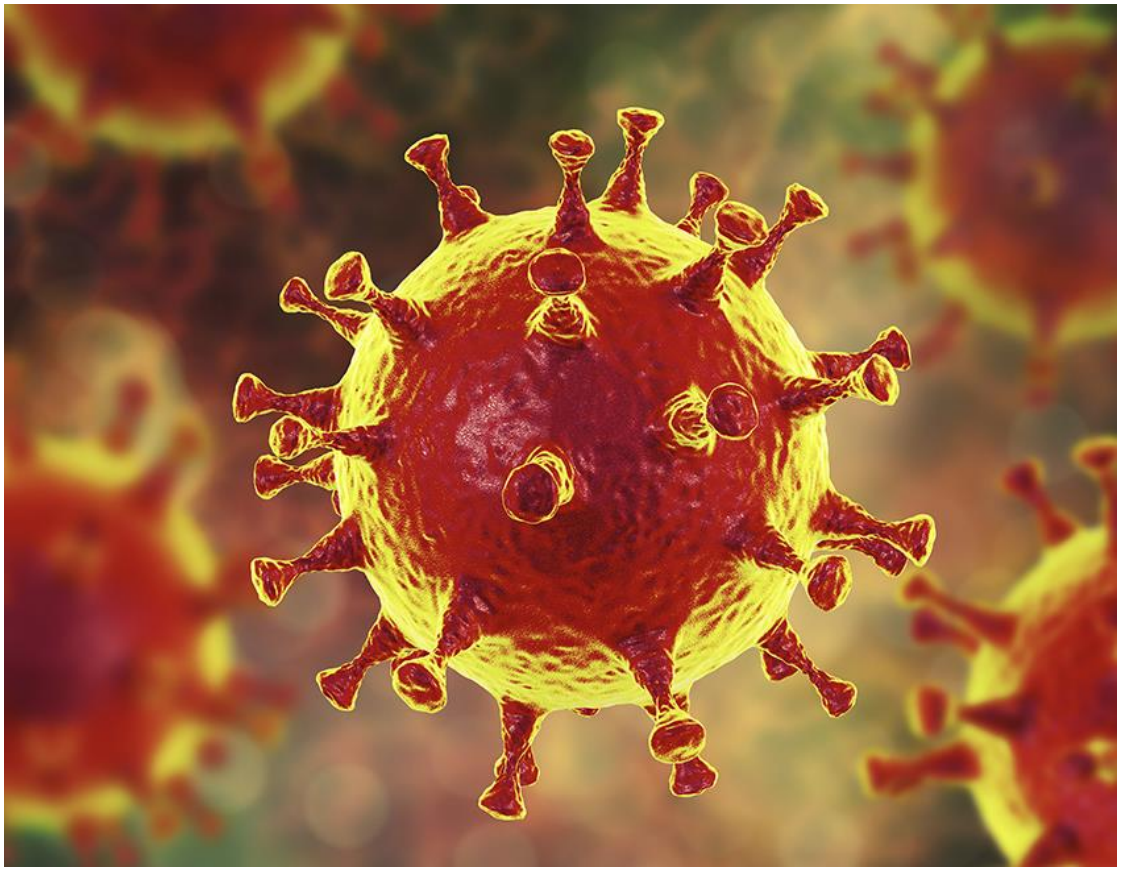
Typical COVID-19 Finger Prick Antibody Assay





COVID-19 Antibody Response

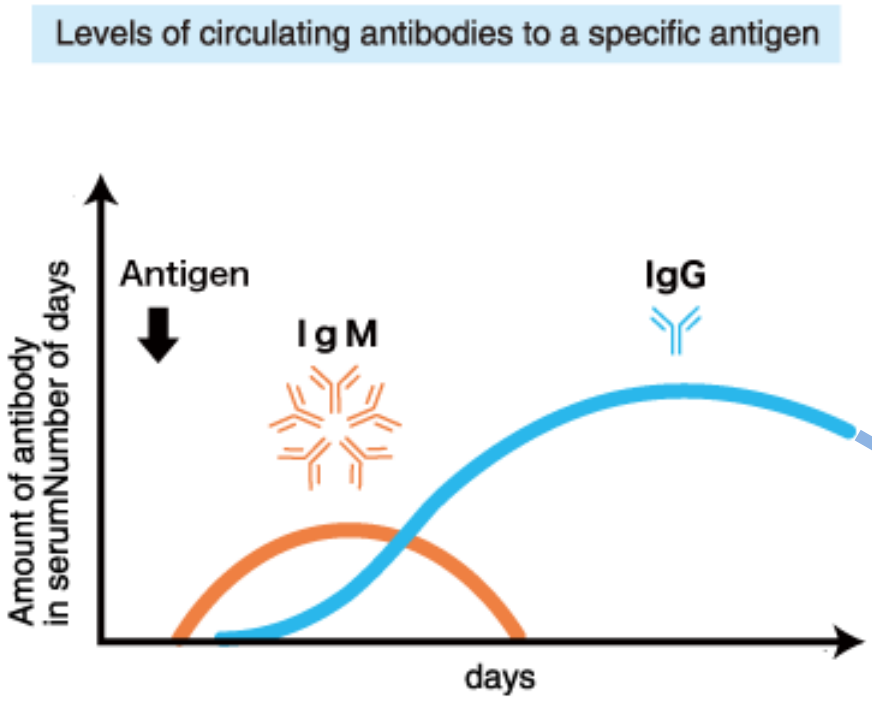
- Studies so far indicate about 50% of people have detectable antibodies within 7 days of infection
- Most within 14 days of infection
- Growing evidence some people do not develop robust antibody response
- Either no antibodies or too few to detect
- May correlate with illness severity



COVID-19 Antibody Response

- ***<u>Much</u> is unknown about COVID-19 antibody response***
- **How long does IgM last?**
- **Is the immune response protective? (Do antibodies neutralize?)**
  - **Fully protect**
  - **Partially protect**
- **If so, for how long?**
  - **Does immunity wane?**
- **Experience from other coronaviruses**
- **South Korean reports of possible 2nd infections**

Possible Antibody Response to COVID-19



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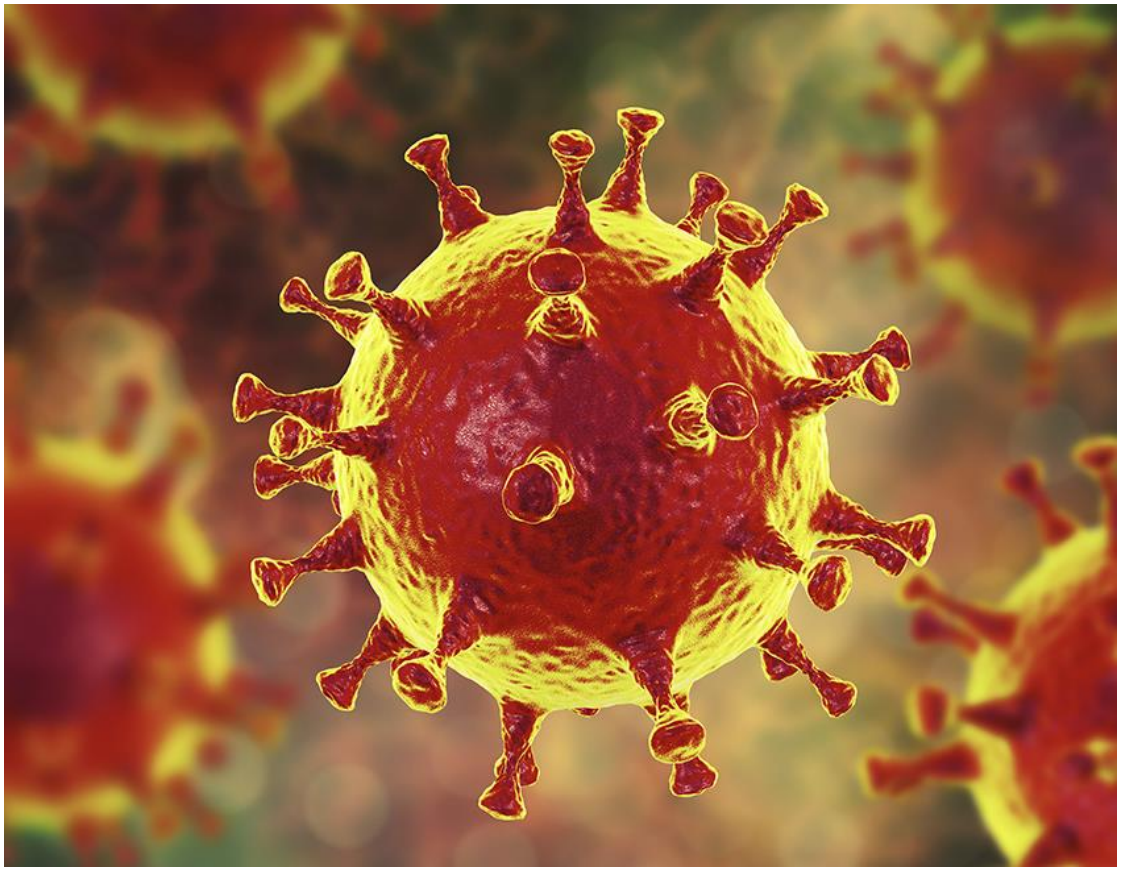
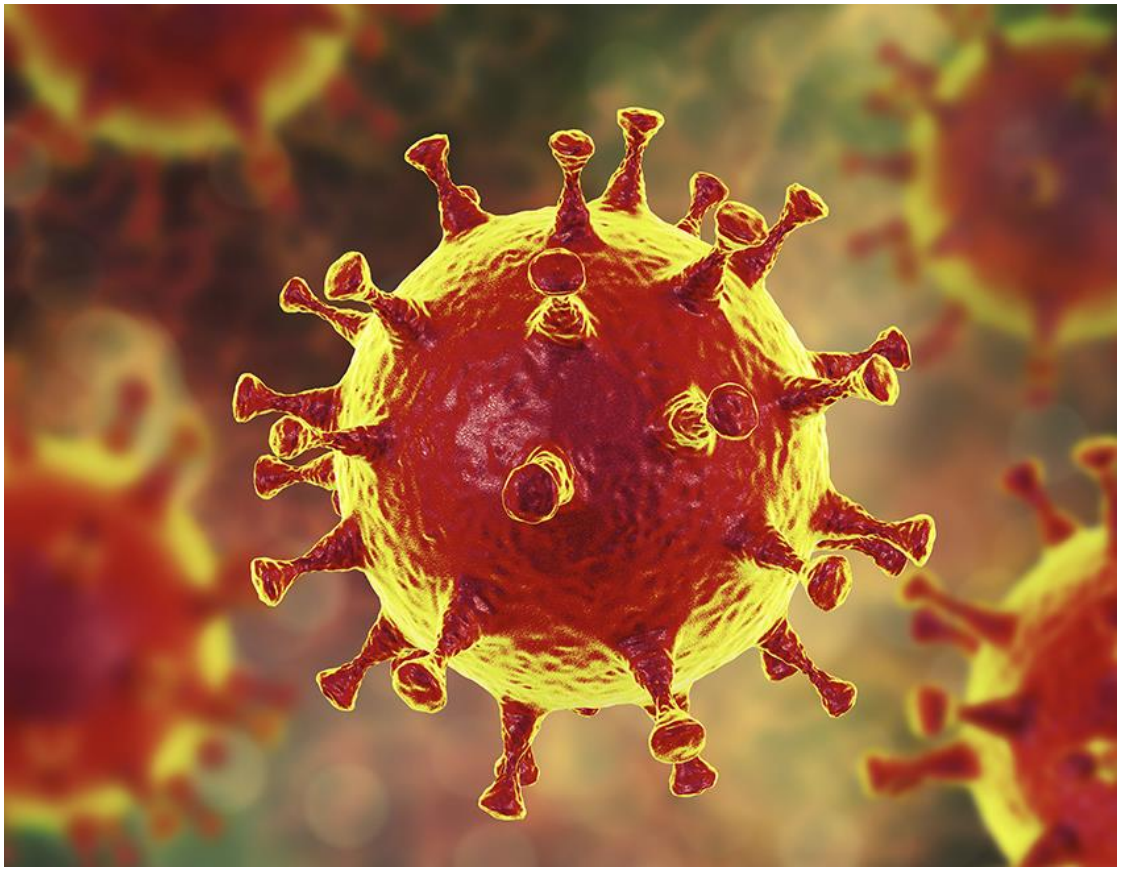


Regulation of Diagnostic Tests

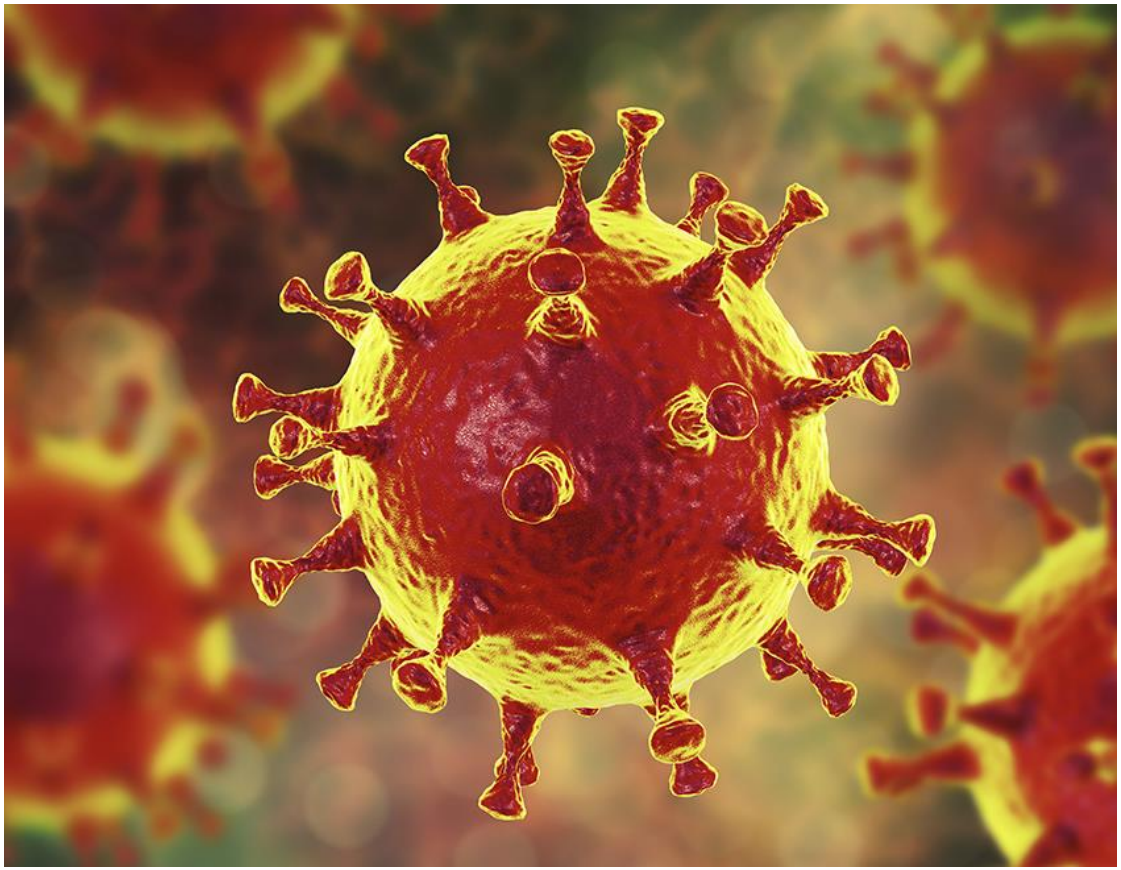
- Diagnostic tests used in humans are considered medical devices
- Regulated by FDA's Center for Devices & Radiologic Health (CDRH)
- Must be approved by FDA for marketing & use*
- Laboratory performing test regulated by CMS under Clinical Laboratory Improvement Act (CLIA)
- FDA regulates the test; CMS regulates the lab
- FDA also regulates the device used to collect the specimens

* May use enforcement discretion for some tests



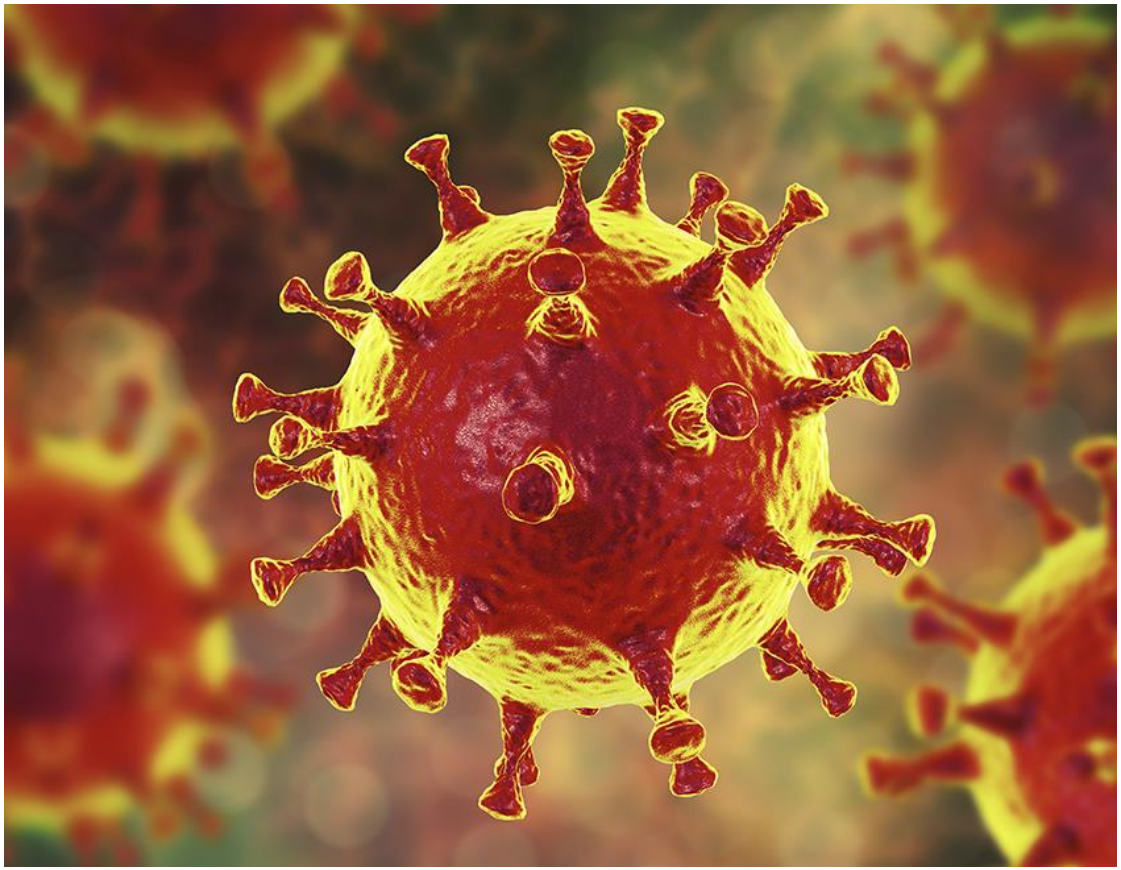
Test Characteristics

- Rare for a diagnostic test to be 100% accurate – although that's ideal
- Critical performance characteristics:
- Sensitivity – how often the test is positive when patient has COVID-19
- Specificity – how often the test is negative when the patient doesn't have COVID-19
- <100% sensitivity = false negative
- <100% specificity = false positive



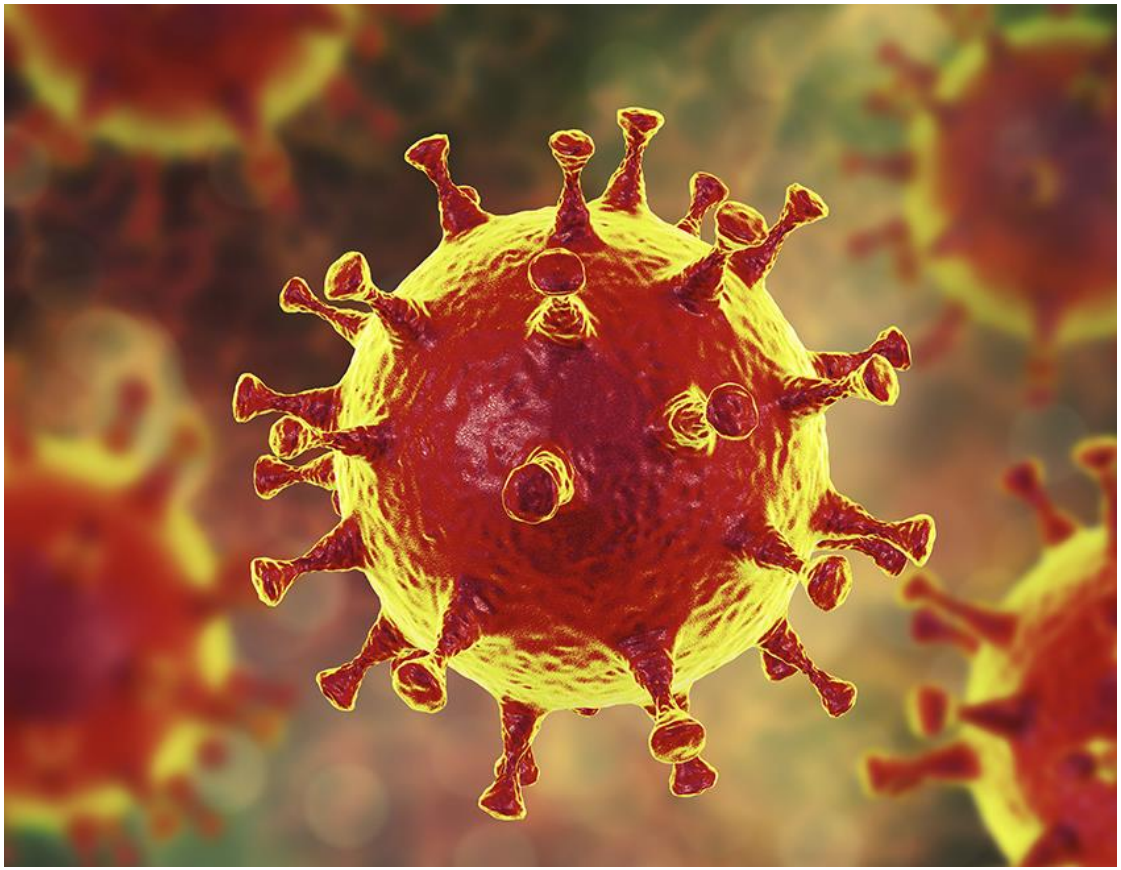
Emergency Use Authorization (EUA)

- In declared emergency, FDA can allow regulated products to be authorized for use without formal approval
- Manufacturer has to submit information regarding product and its performance prior to EUA issuance
- After problems with CDC test, FDA waived EUA requirement if manufacturer:
  - Does validation
  - Later submits EUA request
- Waived for both PCR and antibody tests



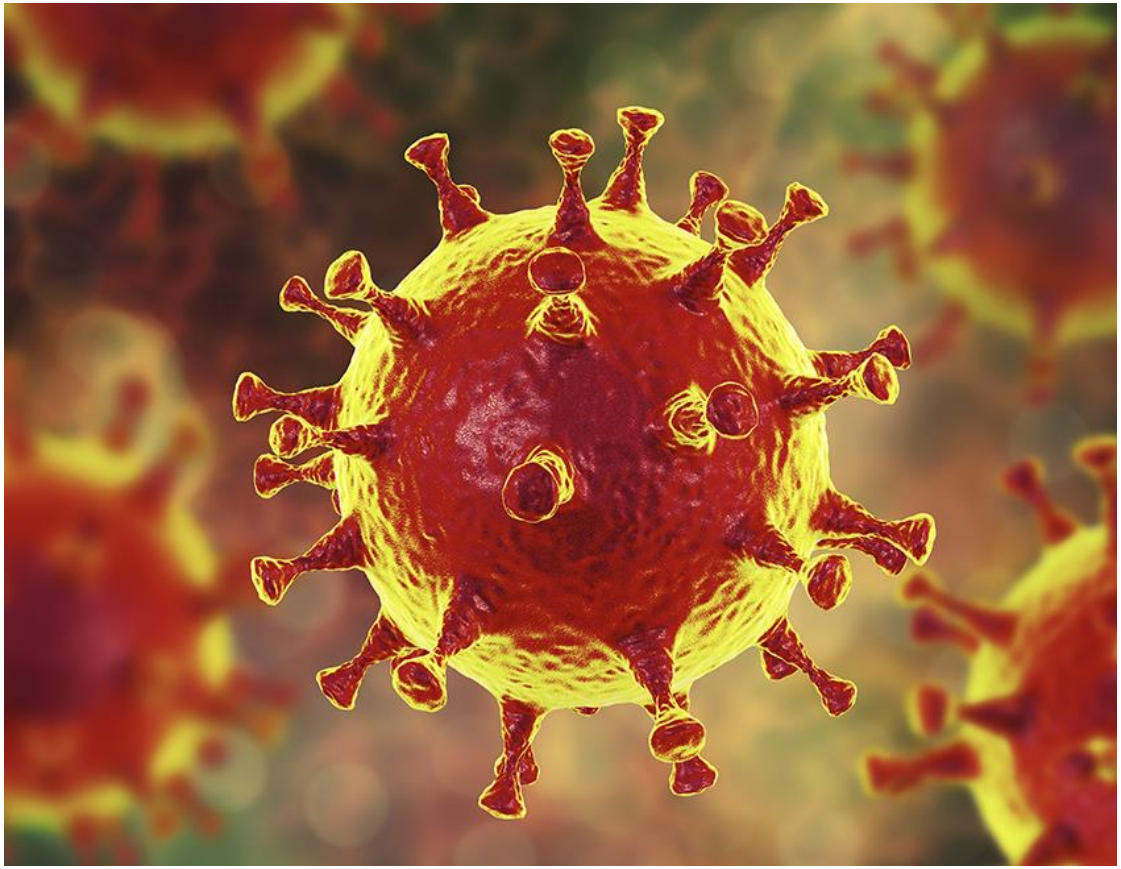
PCR Assay Performance

- There are now two classes of PCR tests available:
  - Standard tests
  - Rapid, point-of-care tests
- Multiple tests in both categories have received EUAs; others on the market have not
- Total 62 EUAs issued (as of Apr 27)
- PCR generally has high sensitivity and specificity
- However, studies have shown can have low sensitivity (70-85%)
- Low sensitivity for acute disease is a significant problem
- Note: antigen capture tests generally have lower sensitivity



Antibody Tests

- Antibody tests have flooded the marketplace
- Many from overseas
- Several different technologies
- Eight EUAs issued (Apr 27)
- Evaluations have shown problems with sensitivity & specificity
- In low prevalence locations, higher % of positive tests may be false positives
- Being used for serosurveys
- Used to identify best donors for convalescent plasma (quantitative test)



Antibody tests

- Can antibody tests be used for individual decision making?
- "Immunity Certificates"
- **False positives can have serious consequences!**
  - **Believe can't be infected**
  - **Adherence to prevention measures**
- CDC blueprint mentions paired antibody tests to improve accuracy
- Even if true positive
  - Don't fully understand immune correlates of protection
  - Immunity may wane
  - Test can't tell you when someone was infected

Take Home Messages

- Challenges with tests for acute infection and with antibody tests
  - Buyer beware for antibody tests
  - This situation likely to improve over time
- Unanswered questions regarding immune response
  - Likely many of these questions will be answered over coming weeks/months
- ***Caution urged about how antibody tests are currently used***

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QUESTIONS?

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THANK YOU!

Coronavirus@idfa.org