Laboratory Testing for COVID-19

ECHO Presentation

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Because there is Strength in Unity

Today's Talk

- FDA Emergency Use Authorization
- Molecular Testing
- Abbott ID NOW
- Antibody Testing
- What's on the Horizon
- What should we be doing?

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FDA Emergency Use Authorization (EUA)

- Not the same as full FDA approval
- Can only be issued during a declared Public Health Emergency that has been authorized by the Secretary of Health and Human Services
- Only valid during the period of emergency
- FDA does a risk vs. benefit analysis to determine if new product is most likely safe and effective

Tests for SARS-CoV-2/COVID-19 and Potential Uses

Type of Test	Measure	Value	Beneficiary
Nucleic acid amplification test for viral RNA *(nasopharyngeal swab, oropharyngeal swab, sputum, bronchoalveolar lavage fluid, others)*	Current infection with SARS-CoV-2	• Inform individual of infection status so they can anticipate course of illness and take action to prevent transmission • Inform patient management and actions needed to prevent transmission • Inform actions needed to prevent transmission	• Individual • Healthcare or long-term care facility • Public health
Antibody detection	Past exposure to SARS-CoV-2	• Detect susceptible individuals (antibody negative) and those previously infected • Identify individuals with neutralizing antibodies • Facilitate contact tracing and surveillance	• Identify those potentially immune to SARS-CoV-2 (if tests can detect protective immunity, individuals could be returned to work) • Healthcare facilities: Experimental therapy • Public health

Robin Patel et al. mBio 2020; doi:10.1128/mBio.00722-20

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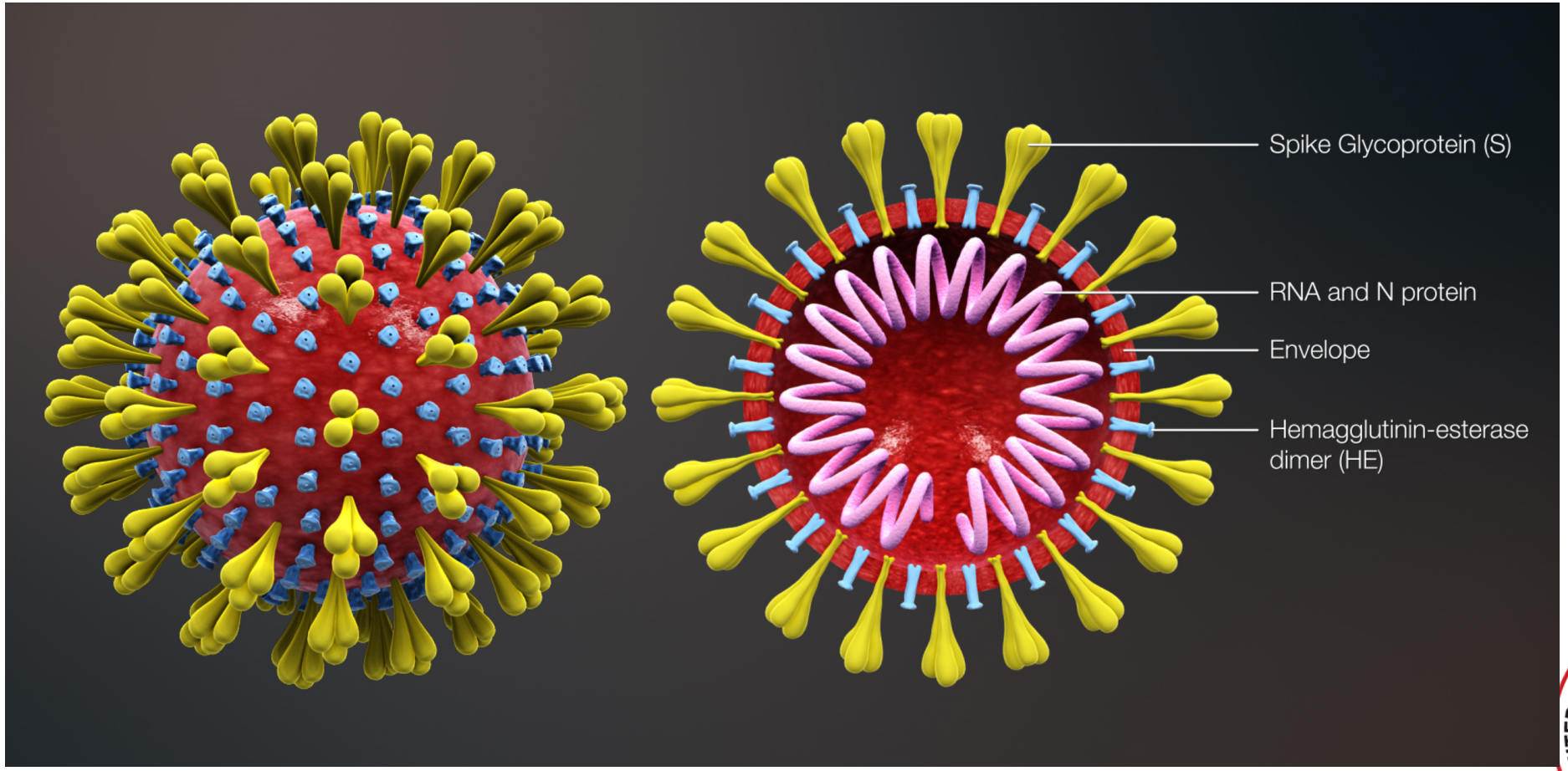
Molecular Testing

When it comes to COVID-19, these are all names for testing for the presence of virus:

- Molecular Testing
- Nucleic Acid Amplification Test
- PCR – Polymerase Chain Reaction (RT-PCR)
- RNA Test
- Viral Particle Test
- Viral Nucleic Acid Test

SARS-CoV-2 Structure



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What is PCR?

- Polymerase Chain Reaction is a Nucleic Acid Amplification process
- PCR is a method to identify a specific gene or genes
- RT-PCR is used for RNA viruses
- Usually requires expensive equipment and a sophisticated laboratory to perform
- Usually takes 2 to 8 hours to perform the test because of multiple thermal cycles

PCR Sensitivity and Specificity

- PCR has good sensitivity and specificity when performed correctly
- The actual sensitivity/specificity is unknown, because there isn't really a "gold standard"
- Sensitivity of the test (ability to find infected people) is negatively impacted by (1) low numbers of viral particles in the sample, (2) poor sampling technique, or (3) storage and transportation of the specimen

CLIA-Waived Molecular Tests

There are currently 3 “CLIA-Waived” NAATs with EUA:

1) Cephid Xpert Xpress
2) Abbott ID NOW
3) Mesa Biotech Accula

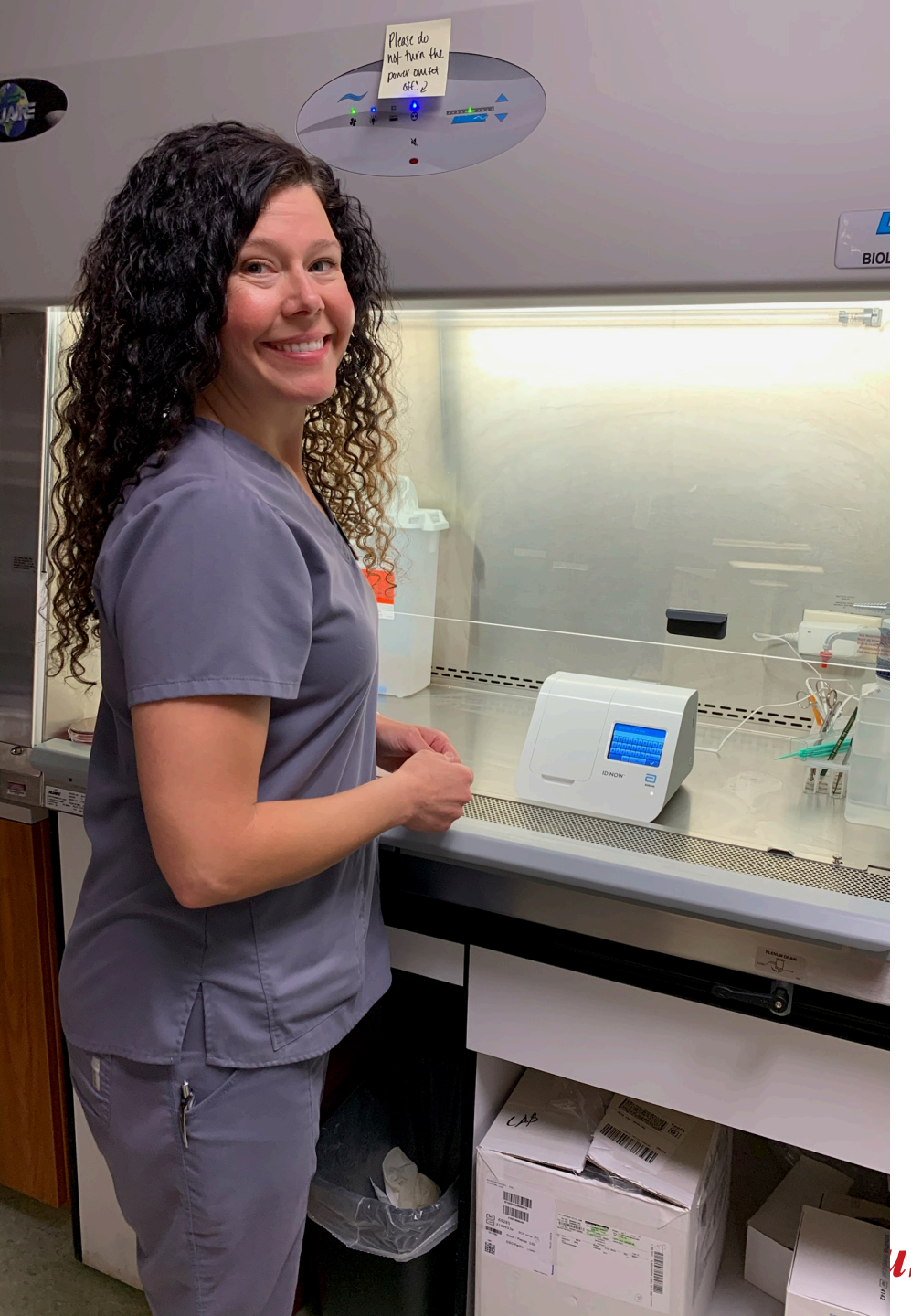
All use faster technology than usual PCR, but basic principle is the same

All claim high sensitivity and specificity

Only Accula was actually tested for cross reactivity

Abbott ID NOW Instrument

- Rapid test that looks for unique piece of viral nucleic acid (region of RdRp gene)
- Isothermal process technology has been used for RSV, influenza, and Group A strep
- Current test cartridges limited
- Sensitivity, specificity is UNKNOWN
- NOT RECOMMENDED for mass screening at this time



Abbott ID NOW Covid-19

- Positive test in as little as 5 minutes
- Negative test in about 13 minutes
- Swab should NOT be put into saline or viral transport media
- High specificity, unknown sensitivity
- LOD (Limit of Detection) 125 copies/mL

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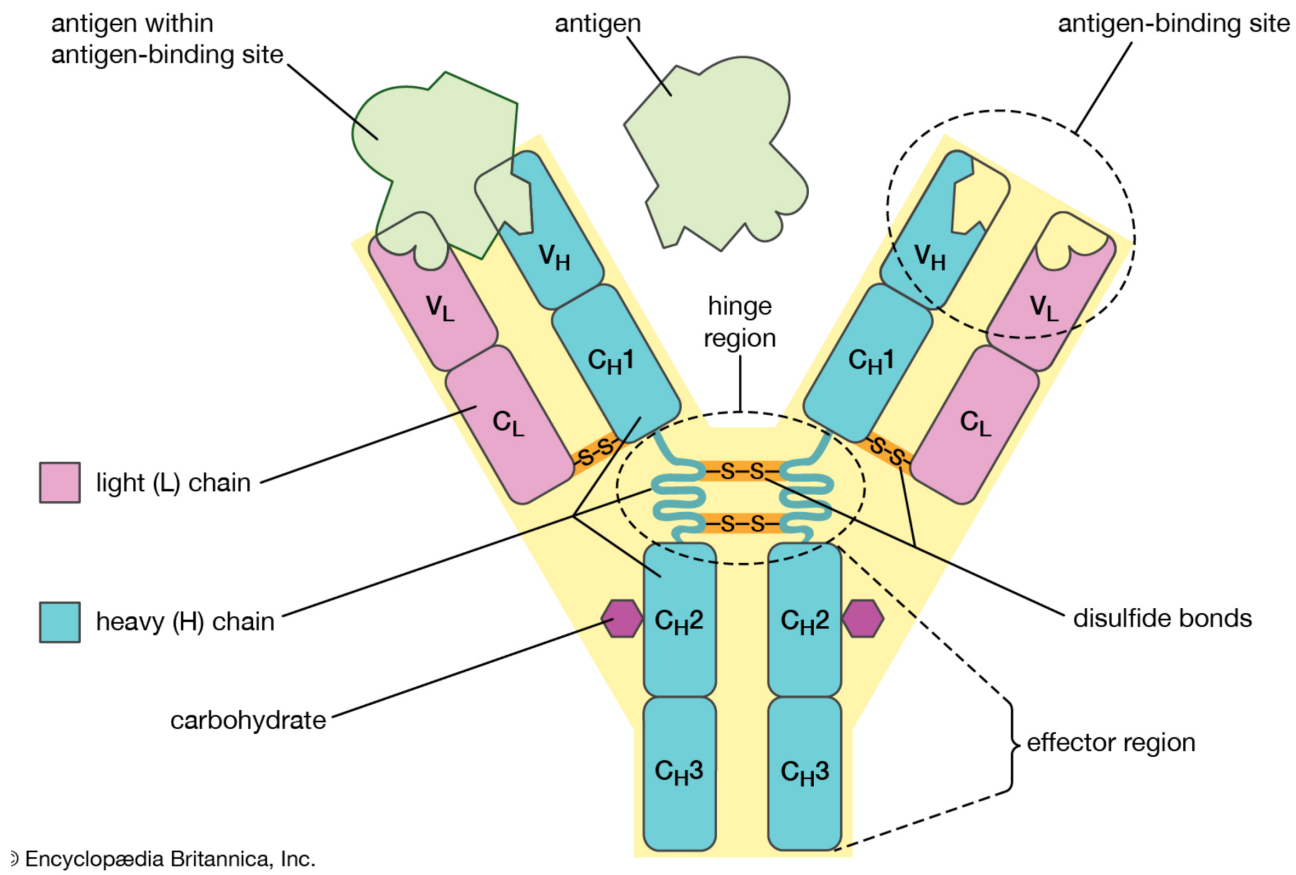
A Brief Review of Immunology

- The body makes antibodies in response to antigens
- Antibodies then bind to antigens to assist in an immune response to get rid of infections or other antigens
- Sometimes antibodies confer immunity, sometimes they do not



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Antibody Testing

- Also known as serology, immunoassay
- Tests for antibodies to SARS-CoV-2
- Not very useful for diagnosing acute infection (may be some situations that it would help)
- Currently is the Wild West – only 12 tests have FDA EUA
- What is the utility of Ab testing?
  - A positive test means that someone was infected
  - High titers during infection correlate with severity
  - A negative test probably means the person was not infected

https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance

Current Antibody Tests with EUA

Company- Test	Type	Antibody (Antigen)	Sens / Spec	Cross Reactivity?
Autobio Diagnostics Rapid Test	Lateral Flow IA	IgM, IgG (Spike)	IgM: 85% / 99% IgG: 86% / 99%	Tested against HCoV Negative for CR
Cellex qRapid Test	Lateral Flow IA	IgM, IgG	94% / 96%	Tested – number not specified
Chembio DPP	Lateral Flow IA	IgM, IgG (Nucleocapsid)	IgM: 77% / 98% IgG: 87% / 93%	Cross reactive with some HCoV
Abbott Architect	Chemiluminescent Microparticle IA	IgG (Nucleocapsid)	100% (>14 days) / 99%	Not tested against HCoV

Current Antibody Tests with EUA

Company- Test	Type	Antibody (Antigen)	Sens / Spec	Cross Reactivity?
BioRad Platelia	ELISA	Total Ab (Nucleocapsid)	92% / 99%	Tested against HCoV Negative for CR
DiaSorin LIAISON	Chemiluminescence Immunoassay	IgG (Spike 1 & 2)	98% (>14 days) / 99%	Tested against HCoV Negative for CR
EUROIMMUN ELISA	ELISA	IgG (Spike 1)	90% / 100%	Tested against HCoV Negative for CR
Mt Sinai Lab	ELISA	IgG (Spike)	92% / 100%	Not tested against HCoV

Current Antibody Tests with EUA

Company- Test	Type	Antibody (Antigen)	Sens / Spec	Cross Reactivity?
Ortho VITROS	Chemiluminescence Immunoassay	IgG (Spike)	88% / 100%	Not tested against HCoV
Ortho VITROS	Chemiluminescence ImmunoAssay	Total Ab (Spike)	83% / 100%	Not tested against HCoV
Roche Elecsys	Chemiluminescence ImmunoAssay	Total Ab (Nucleocapsid)	99% / 100%	Tested against HCoV Negative for CR
Wadsworth NY SARS-CoV	Microsphere Immunoassay	Total Ab (Nucleocapsid)	88% / 99%	Not tested against HCoV

What's on the Horizon?

- Many more molecular and serological tests
- Rapid Antigen Tests
  - Several currently in development (at least 5)
  - Could be great clinical help
  - Sensitivity and Specificity may be lacking

Conclusions

- Right specimen, right time
  - Nasopharyngeal first week, lower resp after first week
- Not all tests are created equal
  - Buyer beware
- Molecular testing for acute infections (for now)
- Antibody tests may be helpful for epidemiology
- Much unknown
  - Does positive serology equal immunity?