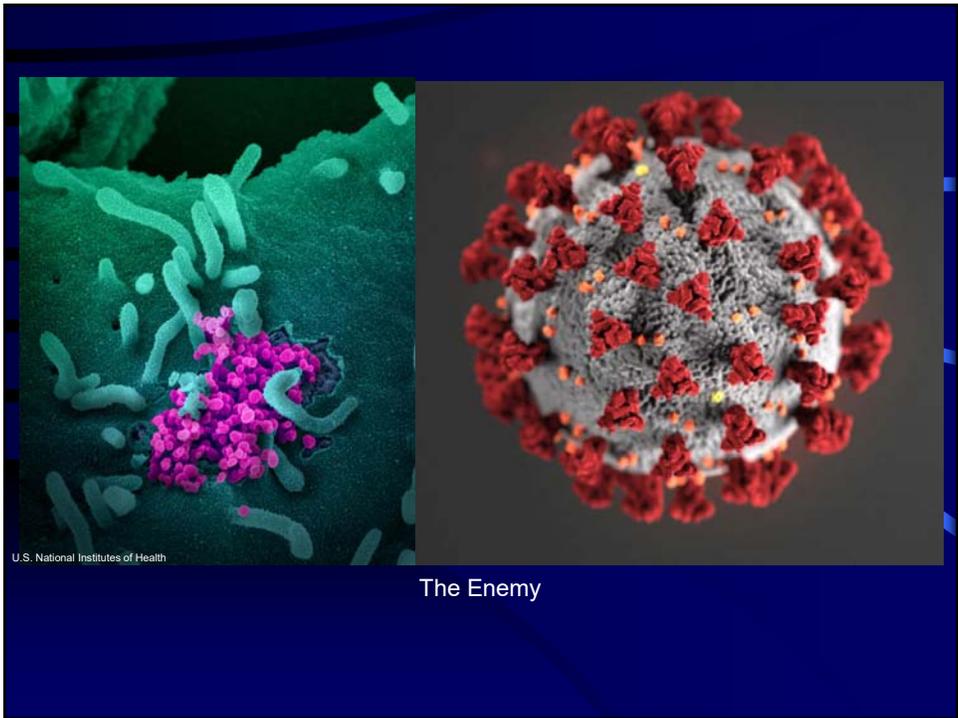


## COVID-19 testing - topics

- Background
  - The virus
  - The epidemic
- Types of tests: nasal swab nucleic acid vs antibody IgG and IgM
- Why test?
  - Differential diagnosis
  - Identification of HCP's, first responders and others with active or resolved infection
  - Identification of infected patients who represent risk to HCP's
- Testing priorities and strategy including contact tracing (containment-mitigation-containment)

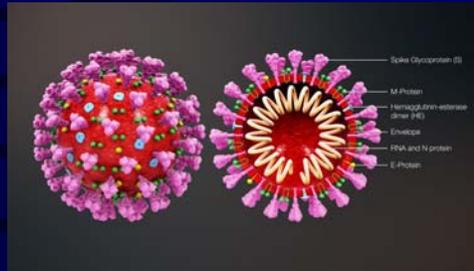


### The virus

- Positive-sense single-stranded RNA (+ssRNA)
- Seen by electron microscopy the virus has a fringe of surface projections creating a “corona” or halo.

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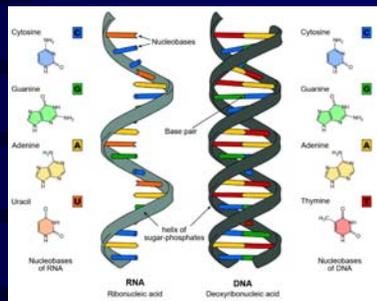
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- Peplomers are glycoprotein spikes on the viral envelope
- Coronaviruses possess the largest genomes (26.4-31.7 kb) among all known RNA viruses
- Virus enters the host cell by binding to ACE2 receptors on the surface of normal cells in the respiratory tract.

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Nucleic acids are RNA and DNA which are composed of nucleotides (or nucleobases) which congregate in 3 base triplets ( $4^3$ ) or 64 codons = 20 (+2) canonical amino acids which form proteins.

“Nucleic acid tests” look for COVID-19 RdRp (RNA-directed RNA polymerase) gene

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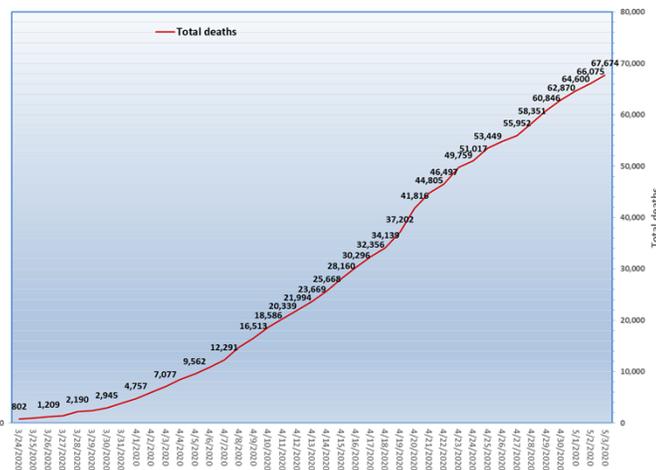
## COVID-19 pandemic

- Disease began in December 2019 in Wuhan, China has since spread globally
- 03 May 2020: >3.5 million cases in 185 countries resulting in >247,000 deaths
- Life Care Center of Kirkland early epicenter for COVID-19 outbreak in the U.S.: 37 people associated with the nursing home died.
- 03 May 2020: >1.1 million cases USA resulting in >67,000 deaths

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COVID-19 Cumulative Deaths U.S.A.



> 72,000 U.S. deaths are anticipated by end of August, 2020

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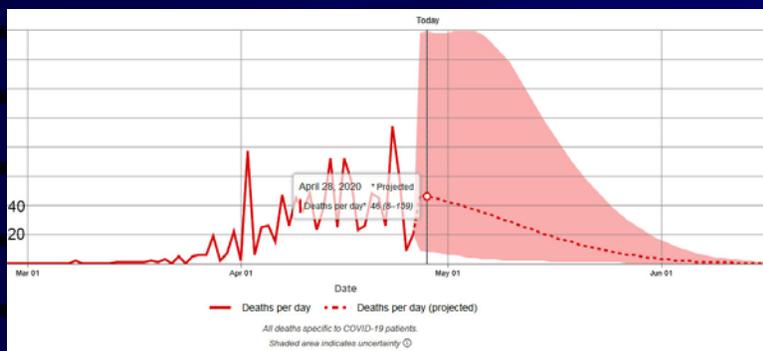
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## US Mortality 2017 = 2,813,503 ≈ 0.86% annual mortality

Rank	Cause of Death	No. of deaths	% of all deaths
• 1.	Heart Diseases	647,457	23.0
• 2.	<b>Cancer</b>	599,108	<b>21.3</b>
• 3.	Accidents	169,936	6.0
• 4.	Chronic lower respiratory diseases	160,201	5.7
• 5.	Cerebrovascular diseases	143,383	5.2
• 6.	Alzheimer disease	121,404	4.3
• 7.	Diabetes mellitus	83,564	3.0
• 8.	Influenza & pneumonia	55,672	2.0

Source: U.S. National Vital Statistics System, U.S. Centers for Disease Control and Prevention, mortality 2017

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Institute for Health Metrics and Evaluation (IHME) of the University of Washington  
 Model run for Florida April 27, 2020, released April 28, 2020

> 1,900 Florida deaths are anticipated by end of August, 2020

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## COVID-19 available tests

- Despite its name, isothermal nucleic amplification or “reverse transcription loop-mediated isothermal amplification (RT-LAMP)” is actually much simpler and faster than RT-PCR for detection of COVID-19 RdRP
- Abbott NOW for “near patient” testing
- Nasal, throat, nasopharyngeal swabs
- Viral transport media (VTM) should not be used



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## Specimen type for available tests - CDC

- Nasopharyngeal (NP) specimen collected by a healthcare professional; or
- Oropharyngeal (OP) specimen collected by a healthcare professional; or
- Nasal mid-turbinate swab collected by a healthcare professional or by a supervised onsite self-collection (using a flocked tapered swab); or
- Anterior nares (nasal swab) specimen collected by a healthcare professional or by onsite or home self-collection (using a flocked or spun polyester swab).

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## COVID-19 available tests

- Technique for nasopharyngeal swab



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## COVID-19 serology tests

Type of test	Time to results	What it tells us	What it cannot tell us	Figure
Rapid diagnostic test (RDT)	10-30 minutes	The presence or absence (qualitative) of antibodies against the virus present in patient serum.	The amount of antibodies in the patient serum, or if these antibodies are able to inhibit virus growth	<a href="#">RDT figure</a>
Enzyme linked immunosorbent assay (ELISA)	2-5 hours	The presence or absence (quantitative) of antibodies against the virus present in patient serum.	If the antibodies are able to inhibit virus growth.	<a href="#">ELISA figure</a>
Neutralization assay	3-5 days	The presence of active antibodies in patient serum that are able to inhibit virus growth <i>ex vivo</i> , in a cell culture system.	It may miss antibodies to viral proteins that are not involved in replication.	<a href="#">PRNT figure</a>
Chemiluminescent immunoassay	1-2 hours	The presence or absence (quantitative) of antibodies against the virus present in the patient serum.	If the antibodies are able to inhibit virus growth.	<a href="#">CLIA figure</a>

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## ABBOTT LAUNCHES COVID-19 ANTIBODY TEST

New test can help determine if someone was infected with the virus and if the person has developed antibodies.



APR 27 2020

Abbott has launched its third test for coronavirus (COVID-19) and is shipping tests to hospitals across the U.S.

The test is a serology test – also called an antibody test – which could be a critical next step in battling this virus.

Abbott's test helps to detect the IgG antibody to SARS-CoV-2. An antibody is a protein that the body produces in the late stages of infection and may remain for up to months and possibly years after a person has recovered. Detecting these IgG antibodies will help determine if a person was previously infected with the virus that causes COVID-19.

The new antibody test is to be used on Abbott's ARCHITECT i2000SR and i2000SR laboratory instruments, which can run up to 100-200 tests an hour.\*

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## • New York State Testing Protocol

- April 26, 2020 NYDOH “Updated Interim Guidance: protocol for COVID-19”: Testing shall be authorized by a health care provider when:
  - An individual is symptomatic or has a history of symptoms of COVID-19 (e.g. fever, cough, and/or trouble breathing), particularly if the individual is 70 years of age or older;
  - The individual has a compromised immune system, or the individual has an underlying health condition; or
  - An individual has had close (i.e. within six feet) or proximate contact with a person known to be positive;

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## • New York State Testing Protocol

- An individual is subject to a precautionary or mandatory quarantine; or
- An individual is employed as a health care worker, first responder, or other essential worker who directly interacts with the public while working; or
- An individual presents with a case where the facts and circumstances – as determined by the treating clinician in consultation with state or local department of health officials – warrant testing.

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## • Goals of nasal swab testing

- Differential diagnosis:
  - During COVID-19 epidemic patients may develop other respiratory infections including influenza and bacterial pneumonia and require specific treatment
- However, certain clinical manifestations are now understood to be strongly suggestive of COVID-19 and testing is not necessary:
  - Rapid onset anosmia
  - Severe bilateral interstitial lung disease with GGO
  - Severe dyspnea and rapid onset hypoxemia
  - Lymphocytopenia, thrombocytopenia, ↑d-dimer

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## • Goals of nasal swab testing

- Management:
  - There is still no effective non-toxic treatment; therefore, positive test does not help select Rx
  - Young generally healthy patients who have mild to moderate disease should stay at home whether their test is positive or negative. Telemedicine and pulse oximetry valuable.
  - Nasal swab nucleic testing should be performed on patients 55+ and those with risk factors for severe outcome (immunocompromise, diabetes, obesity) because positive result will influence admission decision.

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## • Goals of nasal swab testing

- Protecting contacts:
  - It is important to know whether or not a young person who has mild to moderate disease represents a risk to his/her spouse, parents, grandparents, co-workers – therefore, test.
  - Testing should be done to “clear” recovering COVID-19 patients to return to work and/or resume contacts with family especially if they are exposed to high risk individuals including patients; however, Cheng HY JAMA Internal Medicine May 1, 2020 demonstrated that secondary cases did not occur in those who had contact with primary case >6 days after onset of disease in the primary case.

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## • Goals of nasal swab testing

- Protecting contacts:
  - Cheng HY JAMA Internal Medicine May 1, 2020:
    - 100 primary cases, 2761 close contacts, 22 secondary cases (including 4 asymptomatic infections) = infection risk of 0.8% (95% CI, 0.5%-1.2%).
    - Secondary clinical attack rate was 4.6% (95% CI, 2.3%-9.3%) among 151 household contacts and 5.3% (95%CI, 2.1%-12.8%) in 76 nonhousehold family contacts.
    - Among 91 close contacts of 9 asymptomatic cases, no secondary transmission was observed.

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## • Goals of nasal swab testing

- Protecting HCP's:
  - Patients who may require "aerosol generating procedure" i.e. intubation, nebulizer Rx should be tested
  - All pre-op patients including mothers who present for childbirth should be tested
  - Even though HCP's are protected by the use of PPE, patients coming to the ER should be tested

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## • Goals of nasal swab testing

- Protecting HCP's:
  - Patients who may require “aerosol generating procedure” i.e. intubation, nebulizer Rx should be tested
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  - Even though HCP's are protected by the use of PPE, patients coming to the ER should be tested

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## • Goals of antibody testing

- When IgM testing becomes available it will help in early diagnosis
- Detection of IgG suggests protective immunity; however, until further research establishes the degree and duration of immunity, the finding of elevated IgG should not change HCP behavior, i.e. still wear PPE.
- Elevated IgG identifies potential candidate for plasma donation.
- Properly controlled trials of properly selected sample populations will help determine prevalence.

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