

Academy of Medicine of Cincinnati 164th Annual Meeting



Installation Ceremony
COVID-19 Update Webinar

September 16, 2020

Meeting will start promptly at 7:00 pm



Natalie Peterson Executive Director

Thank you for your support

Agenda

- ▶ Welcome - Natalie Peterson, Academy Executive Director
- ▶ Matthew Hardin, MD, Academy Outgoing President
- ▶ COVID-19 Status Report - Where are we now?
 - ▶ Panelists: Stephen Blatt, MD; Thomas Lamarre, MD; Dheeraj Goyal, MD; Lisa Haglund, MD
- ▶ Introduction & Installation of Academy 2020-2021 President - Matthew Hardin, MD
- ▶ Installation of 2020-2021 Academy Council - E. Wyman Morriss, MD
- ▶ Presentation of Medical Student Scholarship - Andrew Markiewitz, MD, Academy Foundation President
- ▶ COVID-19 Panelist Q & A



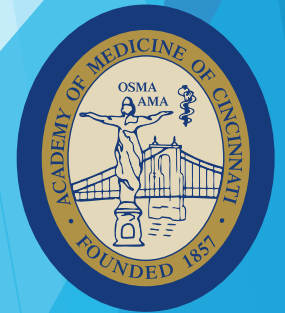
What is the Academy of Medicine of Cincinnati?

- ▶ Founded in 1857, the Academy of Medicine of Cincinnati is a nonpartisan medical society, representing physicians in all medical specialties and practice environments.
- ▶ Not-for-profit, professional association for physicians who practice or live in Hamilton County, Ohio, also serves physicians in surrounding Tri-State counties; physicians in training; and medical students.
- ▶ In 1960, the Academy organized a Foundation, which serves as its philanthropic arm providing grants to local health related organizations. Additionally, it supports Academy educational programs for area physicians and provides an annual \$5,000 scholarship to a 4th year UC medical student.



What does the Academy of Medicine of Cincinnati do?

- ▶ **Advocacy ... Voice**
Speaks out on behalf of physicians on legislative issues
 - ▶ **Community ... Patients**
Links member physicians with patients through member referrals
 - ▶ **Networking ... Education ... Social Activities**
Programs and special events for members and guests. Partners with others in the health care community to support continuing medical education activities.
 - ▶ **Physician Wellness**
As part of the Cincinnati Coalition for Physician Wellness, the Academy of Medicine focuses on prevention and education
 - ▶ **Member Benefits and Services**
Offers a variety of services and benefits for members' professional and personal lives including alliances with local businesses to provide special discounts and savings to members.
- Members who use these offers can recoup the full investment of their dues.





Matthew Hardin, MD

Associate Professor of Internal Medicine
and Pediatrics, University of Cincinnati
College of Medicine

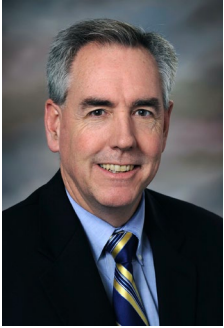
Primary Care Internal Medicine and
Pediatrics, UC Health West Chester Campus

AMC Executive Committee, 2016 - present;
Councilor 2013-present; Finance
Committee; AMC Social Activities Work
Group; and AMC Physician Wellness Work
Group



“COVID-19: Where are we now?”

Panelists



Stephen P. Blatt, MD, FACP
TriHealth

- Medical Director for Infectious Diseases
- System Chief for Medical Specialties



Dheeraj Goyal, MD, MPH
Mercy Fairfield Hospital

- Medical Director, Department of Infectious Diseases
- Chair, Infection Control and Antibiotic Stewardship Committees



Thomas Lamarre, Jr., MD
The Christ Hospital Physicians

- Infectious Diseases



Lisa Haglund, MD, FACP, FIDSA
University of Cincinnati

- Associate Professor of Clinical Medicine
Division of Infectious Diseases



If you would like to submit a question, use the GoToMeeting Question tab

Stephen Blatt, MD

Medical Director for Infectious Diseases
TriHealth

Epidemiology & Symptoms

- ▶ COVID-19 Timeline
- ▶ Current Epidemiology
- ▶ Clinical Manifestations
 - ▶ Presenting signs/symptoms
 - ▶ System Review



COVID-19 Timeline

- ▶ Dec 31, 2019 - WHO reports outbreak of an unusual cluster of pneumonia cases in Wuhan, China - Dr Li Wenliang reports cluster on Dec 30
 - ▶ First case symptom onset Dec 1, 2019, admitted Dec 8
- ▶ Jan 3, 2020 - 44 cases of pneumonia reported in Wuhan with 11 critically ill
 - ▶ Cases seemed to be clustered around a seafood market in Wuhan
- ▶ Jan 10 - WHO publishes checklist to prepare for a novel Coronavirus outbreak
- ▶ Jan 11 - China publishes genetic sequence of the novel Coronavirus
- ▶ Jan 13 - First case reported outside of China in Thailand
- ▶ Jan 30 - WHO declares Public Health Emergency of International Concern
- ▶ Feb 11 - Novel coronavirus disease called COVID-19, virus: SARS CoV-2
- ▶ Mar 7 - 100,000 cases reported worldwide
- ▶ Mar 11 - WHO declares a COVID-19 pandemic
- ▶ Apr 28 - US cases pass 1 million
- ▶ May 9 - Global cases pass 4 million
- ▶ Jun 29 - Global cases pass 10 million

COVID-19 Epidemiology

- ▶ Worldwide cases: 29,030,000
 - ▶ Deaths: 925,000
 - ▶ 1918 Flu Pandemic 500 million cases with 20-50 million deaths
- ▶ US cases: 6,520,000 (We're #1!)
 - ▶ Deaths: 194,000
 - ▶ 1918 Flu 675,000 US Deaths
- ▶ Ohio cases: 137,000
 - ▶ Franklin Co 22,700; Cuyahoga 16,000; Hamilton 11,600
 - ▶ Deaths: 4415

Current R_t

1.00

Cases

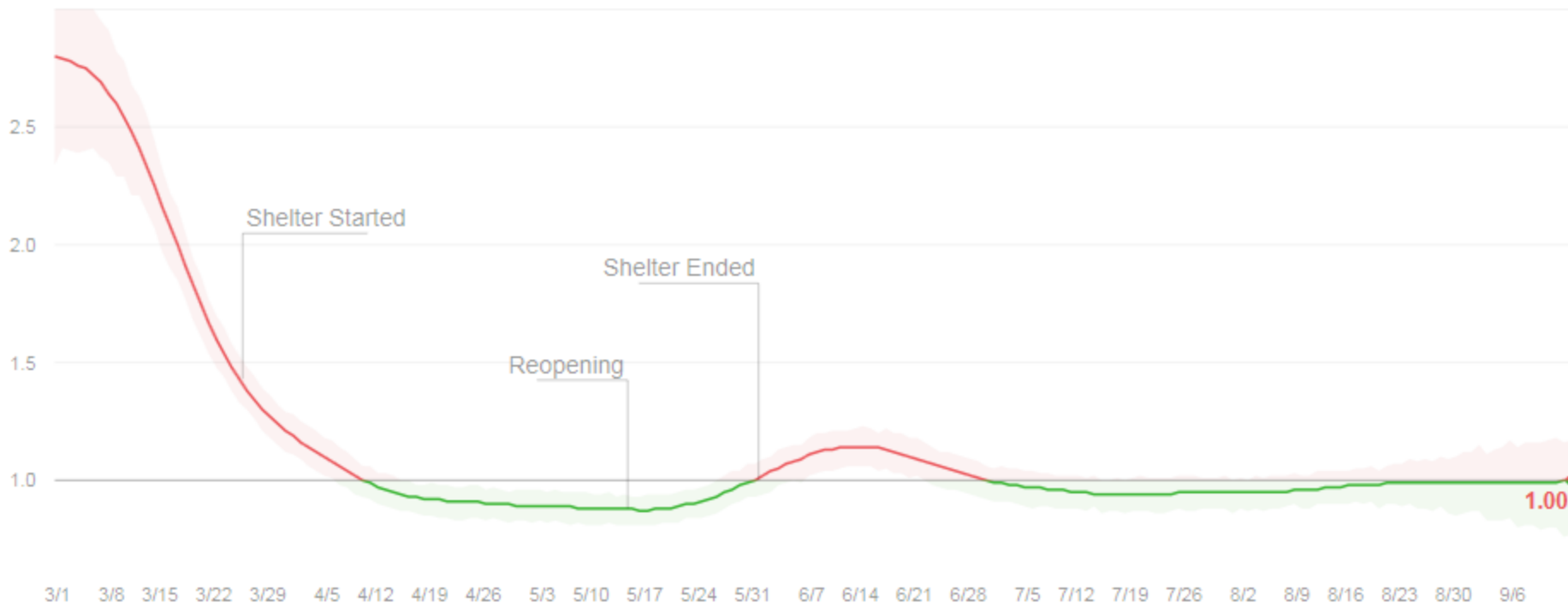
134,342

Tests

2,567,004

Effective Reproduction Rate · R_t

R_t is the average number of people who become infected by an infectious person. If it's above 1.0, COVID-19 will spread quickly. If it's below 1.0, infections will slow. [Learn More](#).



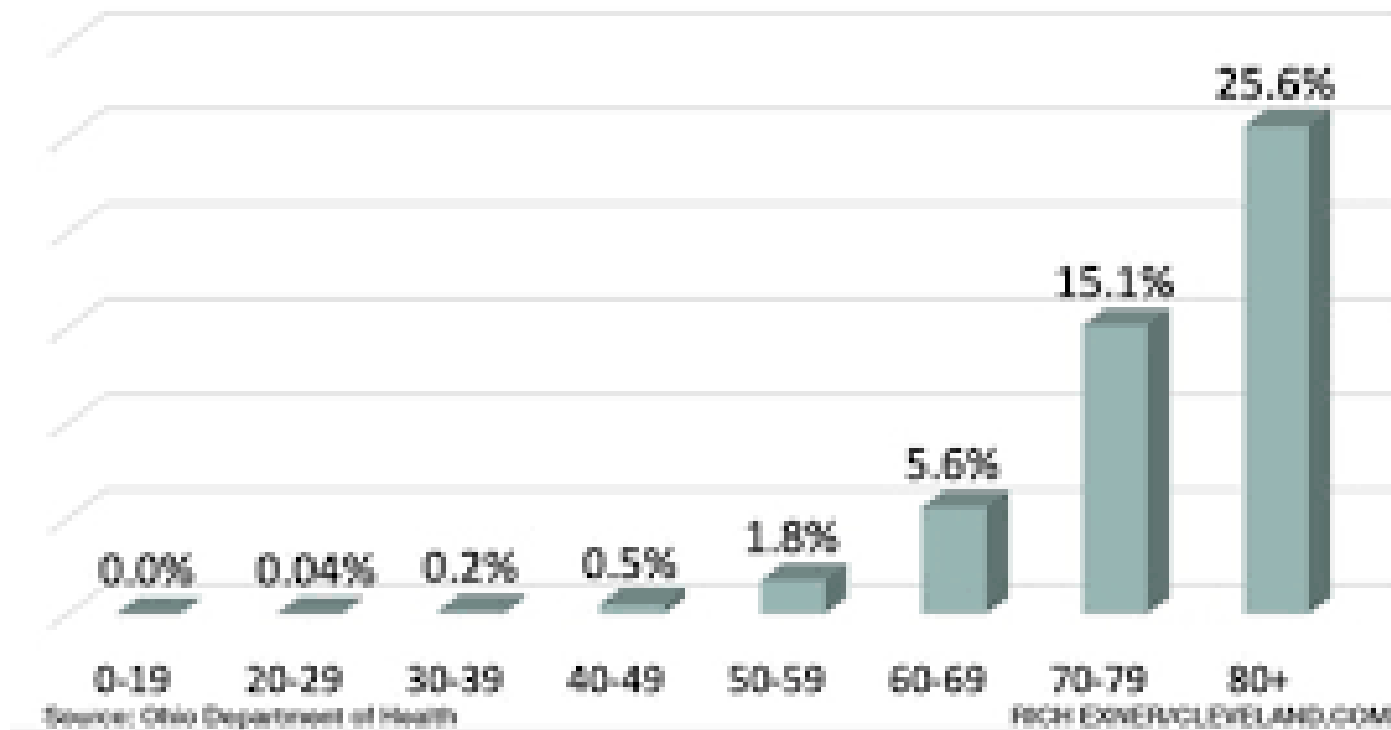
Positive Tests

COVID-19 Fatality Rates

- ▶ Case-fatality rate does not take into account undiagnosed cases
 - ▶ World 3.4%, US 3.1%
 - ▶ Seasonal Flu 0.1-0.2%
- ▶ Infection-fatality rate - determined by doing serosurveys to identify undiagnosed/asymptomatic cases
 - ▶ CDC estimate: 0.26%
 - ▶ IU study of noninstitutionalized community dwelling persons: 0.26%

Ohio Deaths by Age Group

Ohio deaths as a percent of reported coronavirus cases for each age group



COVID-19 Clinical Manifestations

- ▶ Incubation period from exposure to symptom onset 4-5 days
- ▶ Median time from symptom onset to hospitalization 7-10 days
- ▶ Median time to ARDS 8 days
- ▶ Transmission predominantly through droplets exhaled by infectious persons
 - ▶ Transmission beyond 6 ft unlikely
- ▶ Aerosolization may occur under specific conditions
 - ▶ Intubation, singing, “aerosol generating procedures”
 - ▶ May allow virus to travel in air for longer distances and stay suspended in air for longer times
- ▶ Fecal-oral or surface transmission may be possible but not thought to be significant modes of infection

COVID-19 Signs and Symptoms

CDC List

- ▶ Fever/chills
- ▶ Cough
- ▶ Shortness of breath
- ▶ Fatigue
- ▶ Muscle aches
- ▶ Headache
- ▶ Loss of taste or smell
- ▶ Sore throat
- ▶ Congestion, runny nose,
- ▶ Nausea/vomiting
- ▶ Diarrhea

COVID-19 Lab Abnormalities

- ▶ Lymphopenia - 83%
- ▶ Elevated inflammatory markers: ESR, CRP, Ferritin, IL-6, LDH - track the severity of disease
- ▶ Coagulation abnormalities - Prolonged PT, thrombocytopenia, elevated D-dimer, Low fibrinogen
- ▶ Elevated troponin - suggests myocarditis

Radiographic Findings

- ▶ Bilateral lower lobe infiltrates common on chest radiographs
- ▶ Chest CT with ground glass opacities or consolidation in admitted patients (85-100%)
 - ▶ CT findings worsen with disease progression, maximum involvement at day 10 following symptom onset

COVID-19 Complications

- ▶ Pulmonary:
 - ▶ Pneumonia in 75% of hospitalized patients
 - ▶ ARDS - 15%
 - ▶ ICU admission - 17-35%
 - ▶ Mechanical ventilation 30-90%
- ▶ Cardiac:
 - ▶ Elevated troponin - 7-17%
 - ▶ Heart failure
 - ▶ Myocarditis
 - ▶ Arrhythmias

COVID Toes - “Chilblains”



COVID-19 Complications

- ▶ Liver - abnormal LFTs - 25-50%
- ▶ Kidney - AKI 10-25%
- ▶ Neurologic - wide range of reported findings:
 - ▶ CVA - 3%
 - ▶ Encephalopathy - common
 - ▶ Cerebritis/encephalitis - 8-10%
- ▶ Coagulopathy - thromboembolism 10-25%
- ▶ Septic shock - 5-10%
- ▶ “Cytokine Storm” - various definitions in various studies. Associated with more severe disease and worse outcomes
 - ▶ Systemic inflammation characterized by organ injury in the setting of very high inflammatory markers
 - ▶ Multisystem Inflammatory Syndrome in Children (MISC)

Thomas Lamarre, Jr., MD

Medical Director of Infectious Diseases
The Christ Hospital Network

Testing For COVID-19

- ▶ Overview
- ▶ Testing Priorities
- ▶ Nucleic Acid Testing
- ▶ Viral Shedding and Testing Performance
- ▶ Antigen Testing
- ▶ Serologic Testing



OVERVIEW DIAGNOSTIC TESTS FOR SARS-CoV-2

- ALL testing for SARS-CoV-2 has been authorized through the FDA through Emergency Use Authorization (EUA)
- Limited analytic and clinical test performance
 - FDA prefers usage of “natural clinical specimens,” but has permitted use of “contrived specimens”
- Ordinarily test performance studies entail having patients undergo an index test and a “reference standard” test to determine their true state
- “Gold standard” for testing at present is RNA detection
 - NEJM. 2020; 383(6): Epub 2020 Aug 6.

Diagnostic tests for COVID-19^[1,2]

Test category	Primary clinical use	Specimen type	Performance characteristics	Comments
Nucleic acid tests (including RT-PCR)	Diagnosis of current infection	Respiratory tract specimens*	<ul style="list-style-type: none"> ■ High analytic sensitivity and specificity in ideal settings. ■ Clinical performance depends on the type and quality of the specimen and the duration of illness at the time of testing. ■ Reported false-negative rate ranges from <5 to 40%, depending on the test used.[¶] 	<ul style="list-style-type: none"> ■ Time to perform the test ranges from 15 minutes to 8 hours.^Δ ■ Turnaround time is influenced by the test used and laboratory workflow. ■ Some assays allow home collection of specimens that are mailed in.
Serology (antibody detection)	Diagnosis of prior infection (or infection of at least 3 to 4 weeks' duration)	Blood	<ul style="list-style-type: none"> ■ Sensitivity and specificity are highly variable. ■ Detectable antibodies generally take several days to weeks to develop; IgG usually develops by 14 days after onset of symptoms. ■ Cross-reactivity with other coronaviruses has been reported. ■ Individual results should be interpreted with caution in settings of low seroprevalence; serologic tests that have high specificity still have a low positive predictive value. 	<ul style="list-style-type: none"> ■ Time to perform the test ranges from 15 minutes to 2 hours. ■ Turnaround time is influenced by the test used and laboratory workflow. ■ It remains uncertain whether a positive antibody test indicates immunity against future infection.
Antigen tests	Diagnosis of current infection	Nasopharyngeal or nasal swabs	<ul style="list-style-type: none"> ■ Data are limited. ■ Antigen tests are generally less sensitive than nucleic acid tests. 	<ul style="list-style-type: none"> ■ Time to perform the test is <1 hour.

COVID-19: coronavirus disease 2019; RT-PCR: real-time polymerase chain reaction; IgG: immunoglobulin G; CDC: United States Centers for Disease Control and Prevention.

* Nasopharyngeal swabs, oropharyngeal swabs, nasal swabs (from both anterior nares), and nasal or nasopharyngeal washes are recommended by the CDC. Nasal swabs can be self-collected by the patient on-site or at home. Some but not all data suggest that yields from nasopharyngeal specimens are higher than those of other upper respiratory tract specimens. Lower respiratory tract specimens can be collected in hospitalized patients with suspected lower respiratory tract infection if an upper respiratory tract specimen tests negative.

¶ A single positive test generally confirms the diagnosis. If initial testing is negative and clinical suspicion remains, performing a second test can enhance diagnostic yield.

Δ Low-complexity rapid tests can be performed at the point of care and provide results in less than 1 hour. Most moderate- to high-complexity laboratory-based tests result in several hours. However, the time for a clinician or patient to receive a result depends on how frequently the test is run and other processing factors.

References:

1. Cheng MP, Papenburg J, Desjardins M, et al. Diagnostic Testing for Severe Acute Respiratory Syndrome-Related Coronavirus 2: A Narrative Review. *Ann Intern Med* 2020; 172:726.
2. Weissleder R, Lee H, Ko J, Pittet MJ. COVID-19 Diagnostics in Context. *Sci Transl Med* 2020; 12:eabc1931.

PRIORITIES FOR COVID-19 TESTING

- There are no specific clinical features that can reliably distinguish COVID-19 from other viral respiratory infections
- All symptomatic patients with suspected infection should undergo testing
- Testing asymptomatic individuals important for public health or infection control purposes
- Centers for Disease Control and Prevention. Overview of Testing for SARS-CoV-2. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html>.
- Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19, May 5, 2020. <https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics>.

Suggested priorities for SARS-CoV-2 (COVID-19) testing

Priority	IDSA guidance ^[1]
First/High priority	<ul style="list-style-type: none"> ■ Critically ill patients receiving ICU-level care with unexplained viral pneumonia or respiratory failure (regardless of travel or exposure history) ■ Any individual (including health care workers) with fever or features of a lower respiratory tract illness and close contact with patients with laboratory-confirmed COVID-19 within 14 days of symptom onset (including all residents of long-term care facilities with a confirmed case) ■ Individuals with fever or features of a lower respiratory tract illness who are also immunosuppressed (including patients with HIV), older, or have underlying chronic health conditions ■ Individuals with fever or features of a lower respiratory tract illness who are critical to the pandemic response, including health care workers, public health officials, and other essential leaders
Second/Priority	<ul style="list-style-type: none"> ■ Non-ICU hospitalized patients and long-term care residents with unexplained fever and features of a lower respiratory tract illness*[¶]
Third	<ul style="list-style-type: none"> ■ Outpatients who meet criteria for influenza testing (eg, symptoms such as fever, cough, and other suggestive respiratory symptoms plus comorbid conditions, such as diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, age >50 years, immunocompromising conditions); testing of outpatient pregnant women and symptomatic children with similar risk factors is also included in this priority level*
Fourth	<ul style="list-style-type: none"> ■ Community surveillance as directed by public health and/or infectious diseases authorities

These testing priorities refer to testing with RT-PCR (or antigen testing, if available).

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: coronavirus disease 2019; IDSA: Infectious Diseases Society of America; ICU: intensive care unit; RT-PCR: reverse transcription polymerase chain reaction.

* The number of confirmed COVID-19 cases in the community should be considered.

[¶] As testing becomes more widely available, routine testing of hospitalized patients may be important for infection prevention and management at discharge.

References:

1. Infectious Diseases Society of America. COVID-19 Prioritization of Diagnostic Testing. Available at: <http://www.idsociety.org/globalassets/idsa/public-health/covid-19-prioritization-of-dx-testing.pdf> (Accessed on March 26, 2020).

Nucleic Acid Amplification Testing (NAAT)

- ▶ **Detection SARS-CoV-2 RNA from the upper respiratory tract with a reverse-transcription polymerase chain reaction (RT-PCR) assay is the preferred initial diagnostic test for COVID-19**
- ▶ Targets include two or more genes, including the nucleocapsid (N), envelope (E), and spike (S) genes, and regions in the first open reading frame, including the RNA-dependent RNA polymerase (RdRp) gene.
- ▶ **High analytic sensitivity in ideal settings -- they are able to accurately detect low levels of viral RNA in test samples known to contain viral RNA, clinical performance is variable**
- ▶ The CDC recommends collection of one of the following specimens:
 - ▶ Nasopharyngeal swab (or wash / aspirate) specimen, collected by a trained health care professional
 - ▶ Nasal swab (or wash / aspirate) specimen from both anterior nares, collected by a health care professional or by the patient on-site or at home
 - ▶ Oropharyngeal swab specimen, collected by a health care professional
 - ▶ BAL specimen
- ▶ **There is uncertainty regarding the optimal respiratory tract specimen**
- ▶ **Test performance impacted by three primary issues:**
 - ▶ **Sampling - both quality and site of collection**
 - ▶ **Viral shedding dynamics / time of illness**
 - ▶ **Assay type**

▶ MMWR Morb Mortal Wkly Rep. 2020;69(5):140. Epub 2020 Feb 7.

▶ Centers for Disease Control and Prevention. Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19). <https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>.

Site of Collection: Specimen Type

- ▶ Data comparing the accuracy of testing from various sites are limited but suggest that test sensitivity may vary by type of specimen
- ▶ **Lower respiratory tract specimens may have higher viral loads and be more likely to yield positive tests than upper respiratory tract specimens**
- ▶ In a study of 205 patients with COVID-19 who were sampled at various sites, the highest rates of positive viral RNA tests were reported from:
 - ▶ Bronchoalveolar lavage - 95%, 14 of 15 specimens
 - ▶ Sputum - 72% percent, 72 of 104 specimens
 - ▶ Oropharyngeal swab - 32% percent, 126 of 398 specimens
- ▶ Clin Infect Dis. 2020;71(15):793.

Nasal versus Oral Specimen Collection

- ▶ **Some studies have suggested that viral RNA levels are higher and more frequently detected in nasal compared with oropharyngeal specimens**
 - ▶ One study in which 117 pairs of nasopharyngeal and oropharyngeal specimens from 12 patients were tested simultaneously, 32 pairs were discordant with one test positive and the other negative; the nasopharyngeal specimen tested positive in 66% of those pairs compared with 34% for the oropharyngeal specimen
 - ▶ **However, other studies have not identified higher viral RNA levels in nasopharyngeal compared with oropharyngeal specimens**
 - ▶ Prospective study screened 495 asymptomatic healthcare workers with RT-PCR on both salivary and nasopharyngeal specimens
 - ▶ SARS-CoV-2 RNA was detected in salivary specimens; of these 7 matched nasopharyngeal specimens were negative (however, 9 of the 13 patients self collected the nasopharyngeal specimen on the same day)
 - ▶ Second study using primer sequences from the CDC, enrolled 70 inpatients with confirmed COVID-19 (via positive nasopharyngeal swab specimen), evaluated viral detection in matched samples over time
 - ▶ Higher levels of SARS-CoV-2 RNA copies were detected in salivary versus nasopharyngeal specimens
 - ▶ Higher percentage of salivary versus nasopharyngeal specimens were positive up to 10 days after diagnosis (81% versus 71%)
 - ▶ Less variation in RNA levels was also observed in salivary versus nasopharyngeal specimens
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- ▶ Clin Infect Dis. 2020;71(15):793.
 - ▶ Nat Med. 2020;26(6):861. Epub 2020 Apr 23.
 - ▶ Nature. 2020;581(7809):465. Epub 2020 Apr 1.
 - ▶ NEJM. 2020; August 28, 2020. DOI: 10.1056/NEJMc2016359

Suboptimal Biologic Sampling a Probable Cause of False Negative NAAT

- ▶ Study using droplet digital polymerase chain reaction (ddPCR) demonstrated that human DNA levels - a stable molecular marker of sampling quality - were significantly lower in samples of 40 confirmed or suspected COVID-19 cases that were falsely negative
 - ▶ Based on nasopharyngeal swab collection
 - ▶ **Study supports that suboptimal biological sampling - and not just PCR sensitivity - contributes to false negative COVID-19 test results**
 - ▶ The CDC 2019-nCoV real-time RT-PCR diagnostic panel does utilize a human RNaseP RNA-specific primer/probe set to assess sample quality
 - ▶ Study did not address SITE of collection
- ▶ J Infect Dis. 2020; 222(6): 899. 2020 Sept 15.

Viral Shedding, Time of Illness and Detection of SARS-CoV-2

- ▶ It is unknown how soon viral RNA can be detectable following exposure and infection
 - ▶ The highest risk of viral transmission and detection appears to be early in the course of illness
 - ▶ The minimum dose of virus that can initiate infection remains unknown
 - ▶ The precise interval during which an individual with SARS-CoV-2 infection can transmit infection to others remains unknown
 - ▶ The potential to transmit and detect SARS-CoV-2 begins prior to the development of symptoms and occurs in presymptomatic individuals
 - ▶ Transmission may occur in asymptomatic individuals
 - ▶ Transmission after 7 to 10 days of illness appears unlikely, however, NAAT may remain positive for months
 - ▶ Positive testing does not necessarily correlate with infectivity
-
- ▶ N Engl J Med. 2020;382(12):1177. Epub 2020 Feb 19.
 - ▶ Lancet Infect Dis. 2020;20(5):565. Epub 2020 Mar 23.
 - ▶ Nature. 2020;581(7809):465. Epub 2020 Apr 1.
 - ▶ Jama. 2020; 324 (8): 719. 2020 Aug 25.

Peak Viral Shedding and Detection

- ▶ **NAAT performance best defined during interval of peak viral shedding, but much uncertainty**
- ▶ **Viral load in the upper respiratory tract appears to peak around the time of symptom onset**
 - ▶ Viral shedding begins approximately 2 to 3 days prior to onset of symptoms
 - ▶ There is data that viral RNA levels are high prior to the development of symptoms
- ▶ One study evaluated RT-PCR performance by time since symptom onset or exposure with the estimated rates of false-negative results:
 - ▶ 100 percent on the day of exposure
 - ▶ 38 percent on day 5 (estimated as the first day of symptoms)
 - ▶ 20 percent at day 8
 - ▶ 66 percent at day 21
- ▶ Another study used a combination of RT-PCR and an IgM serologic test to make the diagnosis of COVID-19 and suggested that RT-PCR false negative rates were:
 - ▶ <10 percent on days 1 to 3 of illness
 - ▶ >20 percent at day 6
 - ▶ >50 percent after day 14

▶ Nat Med. 2020;26(5):672. Epub 2020 Apr 15.

▶ MMWR. 2020; 69(14):411.

▶ Clin Infect Dis. 2020; Euro Surveill. 2020; 25 (17). 2020 Mar.

▶ Ann Intern Med. 2020;173(4):262. Epub 2020 May 13.

Asymptomatic Transmission and Detection

- ▶ **Testing characteristics and NAAT performance in asymptomatic individuals remains unknown**
 - ▶ **Viral shedding and transmission dynamics in asymptomatic persons remains unknown**
 - ▶ There is data to suggest levels and duration of viral RNA in the upper respiratory tract of asymptomatic patients are also similar to those of symptomatic patients
 - ▶ Multiple studies and reports have described rates of asymptomatic infection ranging from 4 to 32%
 - ▶ Unclear whether these reports represent:
 - ▶ Actual asymptomatic infection in individuals who never develop symptoms
 - ▶ Transmission in individuals with very mild symptoms
 - ▶ Transmission in presymptomatic individuals
 - ▶ A systemic review on this topic suggested that true asymptomatic infection may be uncommon
-
- ▶ Emerg Infect Dis. 2020; 26(8).
 - ▶ JAMA Intern Med. 2020.
 - ▶ MedRxiv. 2020; Preprint posted 2020 June 4.
 - ▶ Lancet Infect Dis. 2020 Epub 2020 June 12.
 - ▶ Emerg Infect Dis. 2020;26(7) Epub 2020 Jun 21.

Prolonged “Viral Shedding” and Detection

- ▶ **Prolonged viral RNA detection does not indicate prolonged infectiousness**
 - ▶ Duration of test positivity may correlate with severity of illness
- ▶ In some individuals, viral RNA can be detected from the respiratory tract months after the initial infection
- ▶ **The Centers for Disease Control and Prevention (CDC) suggests against retesting individuals who were previously diagnosed with SARS-CoV-2 within the prior three months because of the low likelihood that a repeat positive test during this interval represents an active reinfection.**
 - ▶ Detectable viral RNA, however, does not always indicate the presence of infectious virus, and there appears to be a threshold of viral RNA level below which infectiousness is unlikely
 - ▶ Several studies suggest that viral cultures are generally negative 8 days after symptom onset
- ▶ JAMA. 2020; 324(8): 719. 2020 Aug 25
- ▶ Clin Infect Dis. 2020.
- ▶ BMJ. 2020;369:m1443. Epub 2020 Apr 21.
- ▶ Nature. 2020;581(7809):465. Epub 2020 Apr 1.

Types of NAAT Assays

- ▶ There are differences in the limit of detection among the major commercial NAAT assays
- ▶ Retesting samples on different platforms may yield conflicting results
- ▶ Point-of-care NAAT assays may not be as sensitive as laboratory-based tests
- ▶ New approaches to NAAT in the detection of SARS-CoV-2
 - ▶ Sample lysis and direct addition
 - ▶ Loop-mediated isothermal amplification (LAMP)
 - ▶ CRISPR
- ▶ US Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Informs Public About Possible Accuracy Concerns with Abbott ID NOW Point-of-Care Test <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-informs-public-about-possible-accuracy-concerns-abbott-id-now-point>.
- ▶ Diagnostic Performance of a Rapid Point-of-care Test for SARS-CoV-2 in an Urban Emergency Department Setting. Acad Emerg Med. 2020.
- ▶ Nature. 2020; 583: 506. 2020 July 23.

Yet Another Unknown: Cycle Threshold

- ▶ The cycle threshold (Ct) refers to the number of cycles in an RT-PCR assay needed to amplify viral RNA to reach a detectable level
- ▶ The Ct value can thus indicate the relative viral RNA level in a specimen -- with lower Ct values reflective of higher viral levels
- ▶ **The clinical application of the Ct is uncertain.**
- ▶ Ct values are not standardized across RT-PCR platforms -- results cannot be compared across different tests.
- ▶ There are yet no clinical studies that have validated use of Ct to guide management
 - ▶ Lower Cycle threshold values may be associated with worse course of illness and outcomes and threshold values may be useful in predicting the clinical course and prognosis of patients.
- ▶ CEBM. COVID-19: Clinical Utility of Cycle Threshold Values. Jefferson T, Heneghan C. <https://www.cebm.net/study/covid-19-clinical-utility-of-cycle-threshold-values/> 2020 Aug 12.

Group Testing

- ▶ High cost, limited throughput, imperfect specificity, lack of access as well as limited test supplies / reagents of molecular tests make them poorly suited to large-scale testing of populations with low expected rates of positivity
 - ▶ Group testing involves screening pools of specimens - when the pool is negative the involved specimens are declared negative
 - ▶ If a pool is positive, retesting subpools or individual specimens may be necessary
 - ▶ No evidence of polymerase chain reaction inhibition utilizing pooled nasopharyngeal specimens
 - ▶ Two studies have confirmed decrease in analytic sensitivity of pooled PCR specimens (as expected in a specimen diluted by negative samples)
 - ▶ Studies ongoing particularly to examine screening of large groups with low expected prevalence of disease (i.e., asymptomatic healthcare workers).
-
- ▶ J Infect Dis. 2020; 222(6): 903. 2020 Sept 15.
 - ▶ JAMA. 2020; 323: 1967.

Antigen Testing

- ▶ Tests that detect SARS-CoV-2 antigen can be performed rapidly -- may be more accessible with a faster time to results than some NAAT.
 - ▶ May be cost beneficial in regards to NAAT
 - ▶ Specimens collected typically with nasal swabs
 - ▶ Point-of care testing possible
- ▶ Data regarding antigen test performance for SARS-CoV-2 are limited
- ▶ **Typically less sensitive and specific than NAAT**
- ▶ A positive or negative antigen test does not confirm or exclude SARS-CoV-2 infection and should be confirmed with NAAT.
- ▶ Antigen testing cannot detect virus at levels as low as NAAT, but may be useful for individuals who are in the early stages of infection when virus replication is at its highest
 - ▶ Some recommend antigenic testing within five days of exposure
- ▶ Also may be useful for repeated screening of individuals in high-risk settings; modelling studies have suggested that if the frequency of testing is high enough, even tests with lower sensitivity could be successfully used to reduce cumulative infection rates
- ▶ Centers for Disease Control and Prevention. Interim guidance for rapid antigen testing for SARS-CoV-2. <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>
- ▶ JAMA Netw Open. 2020;3(7):e2016818. Epub 2020 Jul 1.

Serology: Overview

- ▶ These are binding antibody tests that detect SARS-CoV-2 antigens (nucleocapsid or spike protein) and include tests that can be performed at the point of care and tests that require specialized equipment and trained laboratory personnel
- ▶ **Very limited utility for diagnosis in the acute setting**
- ▶ **Cross-reactivity with other coronaviruses and other viral pathogens remains a potential concern**
- ▶ Obtaining serology three to four weeks after the onset of symptoms optimizes the accuracy of testing -- sensitivity beyond five weeks is uncertain
 - ▶ Patients who previously had SARS-CoV-2 infection
 - ▶ Patients with current infection who have had symptoms for three to four weeks
- ▶ **An assay measuring IgG antibody or total antibody tests rather than IgM antibody, IgA antibody, or IgM/IgG differentiation tests recommended because of their greater accuracy**
- ▶ The CDC also suggests an alternative strategy of using a two-step testing algorithm, in which an initial positive test is confirmed by a second, different antibody assay
- ▶ Centers for Disease Control and Prevention. Interim Guidelines for COVID-19 Antibody Testing in Clinical and Public Health Settings https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html?deliveryName=USCDC_2067-DM29085 (Accessed on May 26, 2020).
- ▶ Hansen KE, Caliendo AM, Arias CA, et al. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Serologic Testing. August 18, 2020 <https://www.idsociety.org/practice-guideline/covid-19-guideline-serology>.
- ▶ BMJ. 2020;370:m2516. Epub 2020 Jul 1.

Serology: Sensitivity

- ▶ Detectable antibodies generally take several days to weeks to develop
 - ▶ The time to antibody detection varies by assay, antibody and target
 - ▶ Sensitivity within different time frames vary substantially
 - ▶ In a systematic review of 38 studies that evaluated the sensitivity of serologic testing by time since symptom onset in patients with COVID-19:
 - ▶ IgM was detected in 23% by one week, 58% by 2 weeks, and 75% by 3 weeks
 - ▶ IgG was detected in 30% by one week, 66% by 2 weeks, and 88% by 3 weeks
 - ▶ Other studies have suggested that the rate of positive IgG approaches 100 percent by 16 to 20 days
 - ▶ Lateral flow assays (which are used for point-of-care tests) are less sensitive than enzyme-linked immunosorbent assays or chemiluminescent immunoassays
-
- ▶ Cochrane Database Syst Rev. 2020;6:CD013652. Epub 2020 Jun 25.
 - ▶ Nat Med. 2020;26(6):845. Epub 2020 Apr 29.
 - ▶ Neutralizing Antibodies Responses to SARS-CoV-2 in COVID-19 Inpatients and Convalescent Patients. AU Wang X, Guo X, Xin Q, Pan Y, Hu Y, Li J, Chu Y, Feng Y, Wang Q SO Clin Infect Dis. 2020.
 - ▶ BMJ. 2020;370:m2516. Epub 2020 Jul 1.

Serology: Specificity

- ▶ Specificity also varies by type of assay, antibody and target
- ▶ In contrast with IgG antibody and total antibody tests, IgM antibody, IgA antibody, and IgM/IgG differentiation tests generally have specificities below 99 percent
- ▶ To maximize the predictive value of the serologic test, assays with high specificity (≥ 99.5 percent) should be used and testing should be reserved for individuals with a high pre-test probability of prior infection
- ▶ In areas of low seroprevalence and / or low pre-test probability of infection, individual results should be interpreted with caution, since in this setting even serologic tests that have high specificity still have a low positive predictive value
 - ▶ In other words, a positive test may be as likely to reflect a false positive as a true positive
- ▶ Hansen KE, Caliendo AM, Arias CA, et al. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Serologic Testing. August 18, 2020 <https://www.idsociety.org/practice-guideline/covid-19-guideline-serology>.

Duration and Immunity of Measurable Antibodies

- ▶ **The duration of detectable antibodies is uncertain**
 - ▶ In one study, IgG levels were noted to decline by a median of 75% from the acute to early convalescent phase of illness
 - ▶ Eight weeks following infection, 40% of asymptomatic patients and 13% of symptomatic patients did not have detectable IgG
 - ▶ In contrast, in another study of 1107 individuals with positive SARS-CoV-2 molecular testing in Iceland, total Ig antibody tests were reactive in 90%, with titers increasing over the first two months after diagnosis and remaining steady for another two months
- ▶ **Serologic correlates of protective immunity have not been defined**
- ▶ **The CDC recommends that results of antibody testing NOT be used to determine rooming arrangements in congregate settings such as dormitories or prisons, make decisions about return to work, or alter work and personal protective equipment requirements for health care workers and first responders**
- ▶ Nat Med. 2020;26(8):1200. Epub 2020 Jun 18.
- ▶ Rapid Decay of Anti-SARS-CoV-2 Antibodies in Persons with Mild Covid-19. AU Ibarrondo FJ, et al. N Engl J Med. 2020.
- ▶ Humoral Immune Response to SARS-CoV-2 in Iceland. AU Gudbjartsson DF, et al. N Engl J Med. 2020.
- ▶ Centers for Disease Control and Prevention. Interim Guidelines for COVID-19 Antibody Testing in Clinical and Public Health Settings <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>.

Dheeraj Goyal, MD, MPH

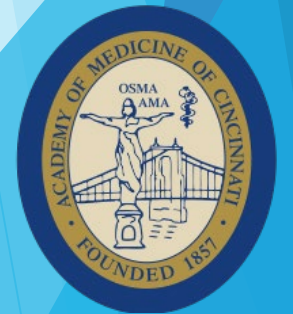
- ▶ Medical Director, Mercy Fairfield Infectious Disease
- ▶ Chair, Mercy Fairfield Infection Control & Antibiotic Stewardship Committees

COVID 19 - Management



Coronavirus Treatment Acceleration Program (CTAP)¹

- ▶ A special emergency program created by Food and Drug Administration (FDA) for possible coronavirus therapies.¹
- ▶ Designed to move new treatments to patients as quickly as possible, while finding out at the same time, whether they are helpful or harmful.
- ▶ Currently, there are no fully FDA approved medications for the treatment of COVID-19.



As of July 31, 2020¹



570+

Drug development
programs in planning
stages¹



270+

Trials reviewed by
FDA²



2

COVID 19 treatments
currently authorized
for Emergency Use

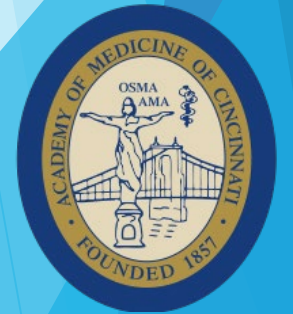


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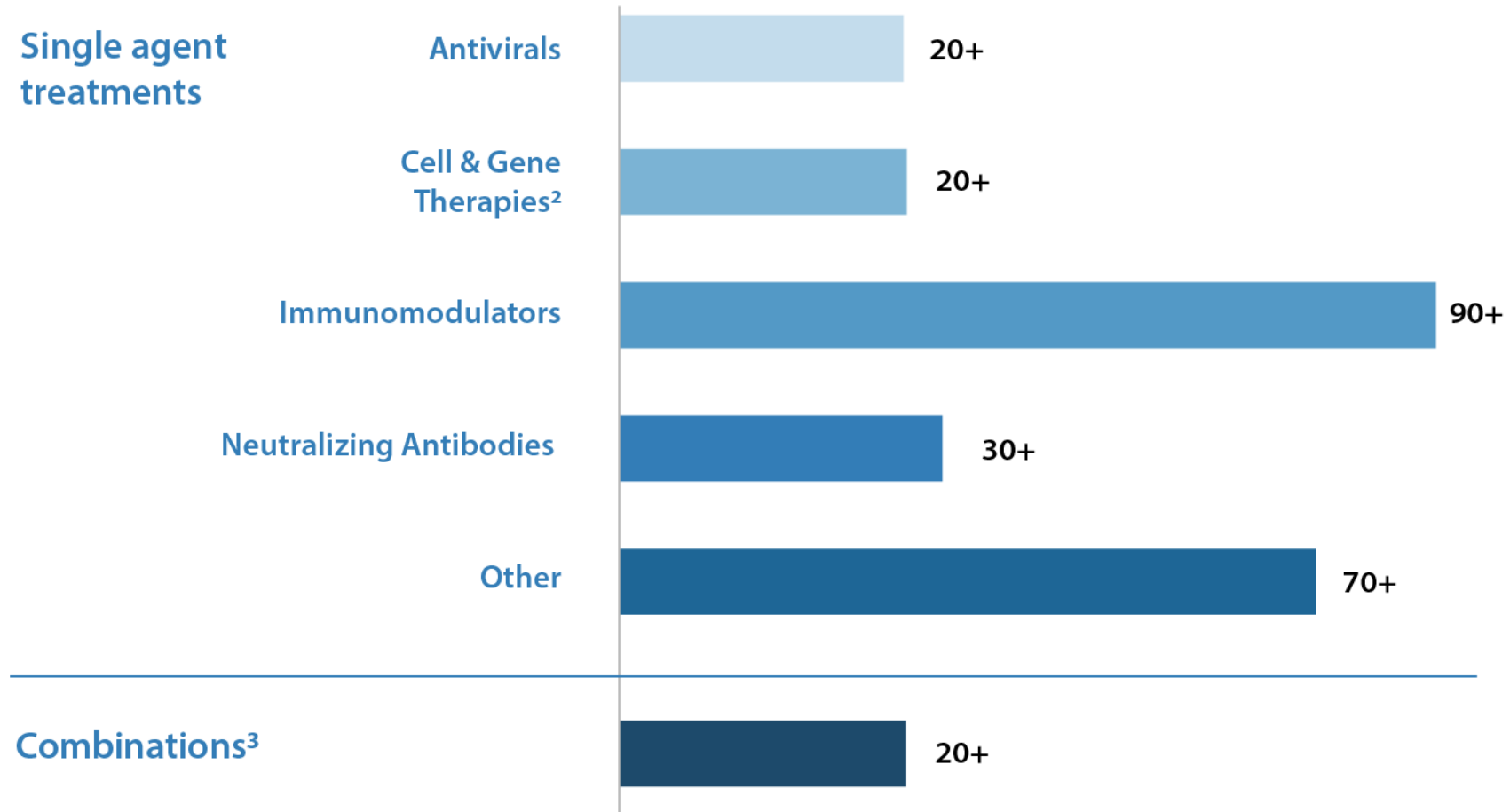
Treatments currently
approved by FDA for
use in COVID-19

¹. Active Pre-INDs. Excludes vaccines.

². Safe to proceed INDs. Excludes vaccines.



Type of COVID-19 Treatment Being Studied¹



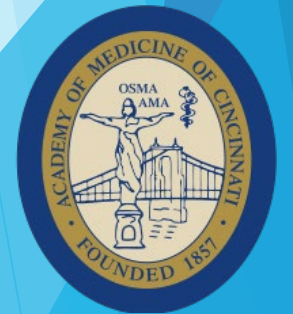
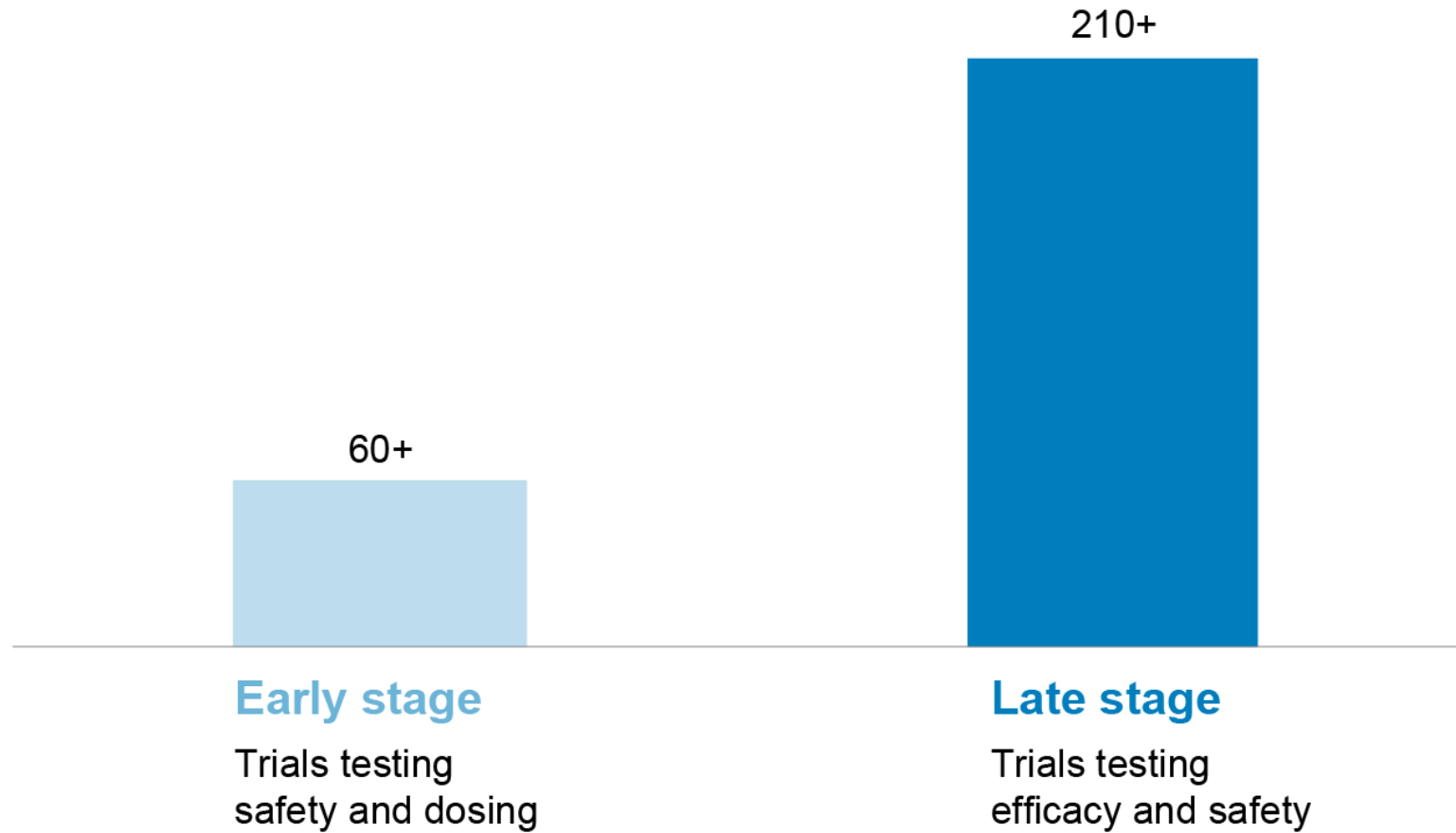
¹ Corresponds to number of safe to proceed INDs. Excludes INDs related to vaccines

² For additional information, please see [Cellular & Gene Therapy Products](#)

³ Includes INDs with more than one product



Stage of COVID-19 Trials in the U.S.



NIH COVID-19 Treatment Guidelines² : Antiviral therapies

REMDESEVIR^{3,4}:

- ▶ For patients who require supplemental Oxygen (but not through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO): Remdesivir for 5 days or until hospital discharge, whichever comes first
- ▶ For patients requiring Oxygen through a high-flow device, NIV (noninvasive ventilation), invasive mechanical ventilation, or ECMO : NIH Panel cannot make a recommendation either for or against starting remdesivir.
- ▶ In patients with mild or moderate COVID-19: Insufficient data for NIH² and IDSA⁵ Panel to recommend either for or against the use of remdesivir.

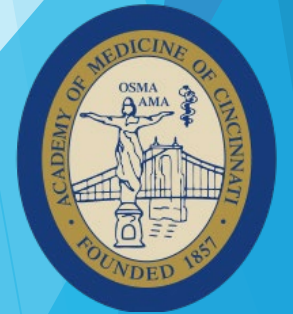


REMDESEVIR ^{3,4}:

- ▶ In patients on **mechanical ventilation or ECMO**, IDSA suggests **10 days of remdesivir**.
- ▶ The **IDSA panel⁵** defines **severe illness** as patients with $\text{SpO}_2 \leq 94\%$ on room air, and those who require supplemental oxygen
- ▶ For **patients with COVID-19 who have not shown clinical improvement after 5 days of therapy**: Insufficient data on the optimal duration. In this group, **some experts extend the total remdesivir treatment duration to up to 10 days** (NIH Panel, CIII recommendation).

Other agents previously thought to have antiviral activity against COVID-19

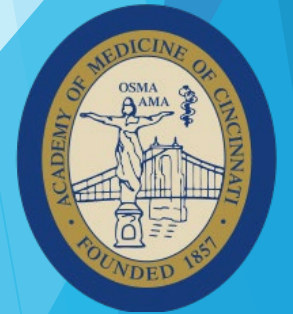
- ▶ NIH & IDSA Panels **recommend against** the use of **chloroquine** or **hydroxychloroquine** for the treatment of COVID-19 in non-hospitalized or hospitalized patients, except in a clinical trial (AI).
- ▶ Both Panels **recommend against** using **hydroxychloroquine plus azithromycin, lopinavir/ritonavir (AI) or other HIV protease inhibitors** as well as **Ivermectin** to treat COVID-19, except in a clinical trial (AIII).



Immune based therapies: Immunomodulators

Corticosteroids:

- ▶ On the basis of data from **Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial⁶**, NIH Panel recommends using **dexamethasone 6 mg per day in hospitalized patients for up to 10 days or until hospital discharge, whichever comes first**, for those who are requiring supplemental oxygen, whether are mechanically ventilated (AI) or not (BI).
- ▶ The Panel **recommends against** using **dexamethasone** for the treatment of COVID-19 in patients **who do not require supplemental oxygen (AI)**.
- ▶ If **dexamethasone is not available**, the Panel recommends using alternative glucocorticoids such as **prednisone, methylprednisolone, or hydrocortisone (AIII)**



Other Immunomodulators in COVID-19 treatment:

- ▶ **Phase 3 COVACTA trial⁶**, a global double-blind placebo-controlled RCT that investigated use of IL-6 inhibitor, **Tocilizumab (Actemra)** in **COVID 19 associated pneumonia**, **did not meet its primary endpoint** of improved clinical outcomes **or the key secondary endpoint** of reduced patient mortality.

NIH Panel recommends against the use of the following, except in a clinical trial:

- ▶ **Anti-IL-6 receptor monoclonal antibodies** (e.g., sarilumab, tocilizumab) or **anti-IL-6 monoclonal antibody** (siltuximab) (BI).
- ▶ **Interferons (alfa or beta)** for the treatment of severely or critically ill patients with COVID-19 (AIII).
- ▶ **Bruton's tyrosine kinase inhibitors** (e.g., acalabrutinib, ibrutinib, zanubrutinib) and **Janus kinase inhibitors** (e.g., baricitinib, ruxolitinib, tofacitinib) (AIII).

Insufficient data to recommend either for or against the use:

- ▶ **Interleukin (IL)-1 inhibitors** (e.g., anakinra)
- ▶ **Interferon beta** for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19.



Immune based therapies: Blood-Derived Products

- ▶ On August 23, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19.⁷
- ▶ Insufficient data for the NIH panel to recommend use of COVID-19 convalescent plasma.
- ▶ It should not be considered standard of care for the treatment of patients with COVID-19
- ▶ COVID-19 specific intravenous immunoglobulins: Insufficient data for the NIH panel to recommend either for or against the use



Other Blood-Derived Products

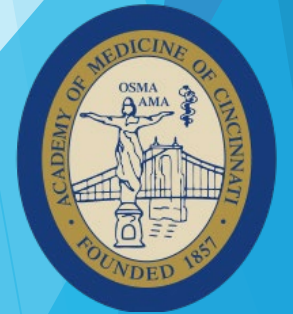
The NIH Panel recommends **against the** use of the following, except in a clinical trial:

- ▶ Mesenchymal stem cells (All)
- ▶ Non-COVID-19 specific intravenous immunoglobulin (IVIG) (All)*.

*(This recommendation should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19.)

Supplemental therapies: Antithrombotic Therapy

- ▶ Continue anticoagulant or antiplatelet therapies for underlying medical conditions (AIII).
- ▶ Do not routinely start preventive anticoagulants and antiplatelet therapy in non-hospitalized COVID-19 patients, unless there are other approved indications (AIII).
- ▶ Insufficient data to recommend either for or against use of therapeutic doses of antithrombotic or thrombolytic agents in hospitalized COVID-19 patients (BIII).
- ▶ Recommendations for routine DVT prophylaxis are the same for hospitalized pregnant and nonpregnant patients with or without COVID-19 infection (AIII).



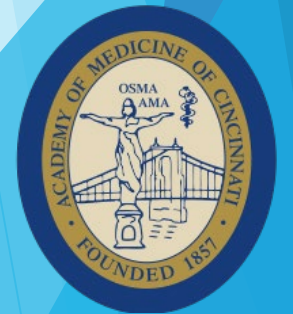
Other supplemental therapies:

- ▶ **Vitamin C, Vitamin D, Zinc:** Insufficient data
- ▶ **ACE inhibitors or ARBs or statins for cardiovascular disease (or other approved indications) should continue (AIII).**
- ▶ **NIH Panel recommends against the use of ACE inhibitors or ARBs or statins for the treatment of COVID-19, except in a clinical trial (AIII).**
- ▶ **No difference in the use of antipyretic strategies (e.g., with acetaminophen or NSAIDs) between patients with or without COVID-19 (AIII).**
- ▶ **IDSA panel recommends against famotidine use for the sole purpose of treating COVID-19 in hospitalized patients, outside of the context of a clinical trial . (Conditional recommendation, very low certainty of evidence)**



Oxygenation and Ventilation in COVID 19

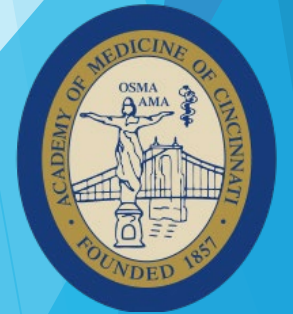
- ▶ **Surviving Sepsis Campaign⁸** suggests starting supplemental oxygen if the peripheral oxygen saturation (Spo₂) is < 92%. Spo₂ should not be maintained higher than 96%
- ▶ For adult COVID-19 patients with acute hypoxemic respiratory failure, the **NIH Panel recommends high-flow nasal cannula (HFNC) oxygen over noninvasive positive pressure ventilation (NIPPV) (BI).**
- ▶ Consider trial of awake prone positioning to improve oxygenation in non-intubated patients with persistent hypoxemia (NIH CIII recommendation), but not as a rescue therapy to avoid intubation in patients, who otherwise require intubation and mechanical ventilation (AIII).



Oxygenation and Ventilation

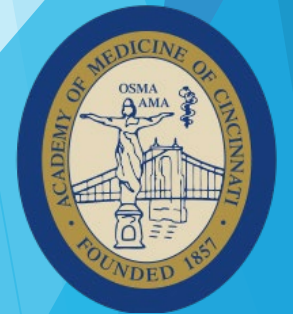
- ▶ For mechanically ventilated adults with COVID-19 and ARDS, NIH Panel recommends:
 - Using low tidal volume (VT) ventilation (VT 4-8 mL/kg of predicted body weight) over higher tidal volumes (VT >8 mL/kg) (AI).
 - Targeting plateau pressures of <30 cm H₂O (AII).
 - Conservative fluid strategy over a liberal fluid strategy (BII).

- ▶ In COVID-19 patients with moderate-to-severe ARDS:
 - The Panel recommends using a higher PEEP (positive end-expiratory pressure) over a lower PEEP strategy (BII).
 - In refractory hypoxemia despite optimized mechanical ventilation, NIH Panel recommends prone ventilation for 12 to 16 hours per day over no prone ventilation (BII).



Oxygenation and Ventilation

- ▶ NIH Panel recommends using continuous infusion or PRN intermittent boluses of neuromuscular blocking agents (NMBA), to facilitate protective lung ventilation (BIII).
- ▶ For mechanically ventilated adults with COVID-19, severe ARDS, and hypoxemia despite optimized ventilation and other rescue strategies, the NIH panel:
 - Recommends using recruitment maneuvers (CII).
 - Recommends using inhaled pulmonary vasodilators as rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off (CIII)
 - Recommends against use of incremental PEEP (staircase PEEP) strategy (All).



References:

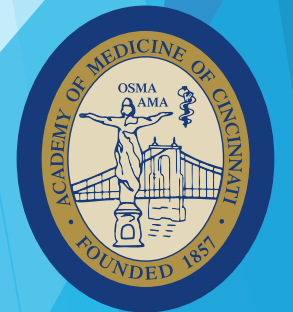
1. <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap>
2. <https://www.covid19treatmentguidelines.nih.gov>
3. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020; 395(10236): 1569-78.
4. Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. N Engl J Med 2020.
5. <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>
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7. Food and Drug Administration. Convalescent plasma letter of authorization. 2020. Available at: <https://www.fda.gov/media/141477/download>. Accessed September 7, 2020.
8. <https://www.sccm.org/getattachment/SurvivingSepsisCampaign/Guidelines/COVID-19/SSC-COVID-19-Guidelines-Microlearning-Ventilation.pdf?lang=en-US>



Lisa Haglund, MD

Viruses and Vaccines

- ▶ Worldwide SARS-CoV2 vaccine effort is underway
- ▶ Sheer case numbers are facilitating vaccine development
- ▶ Expect the unexpected!



Virus 101: Remember “Tropism?”

- ▶ The capability of a virus to infect a distinct group of cells in a host
- ▶ Tropism is determined by the availability of virus receptors on the surface of a host cell
 - ▶ Without the right receptor, a virus cannot infect a host cell
- ▶ Influenza uses receptors on respiratory epithelial cells
- ▶ HIV uses cellular receptor CD4 plus either chemokine receptor CCR5 or CXCR4 on lymphocytes
 - ▶ Berlin patient cured of HIV after bone marrow transplant from donor whose cells lack the CCR5 receptor
- ▶ SARS-CoV1 and SARS-CoV2 use Angiotensin Converting Enzyme II (ACE2)
 - ▶ Heart, kidneys, lung

What are examples of Single-Stranded RNA Viruses?

- ▶ Ebola virus disease
 - ▶ Rabies
 - ▶ Influenza
 - ▶ Polio
 - ▶ Measles
- These have vaccines
- ▶ Rhinovirus (common cold)
 - ▶ Hepatitis E
 - ▶ West Nile fever
 - ▶ Zika
 - ▶ Hepatitis C
 - ▶ HIV
 - ▶ SARS

No vaccines here yet

Why are Single-Stranded RNA Viruses such a Problem?

- ▶ 3 - 4 new RNA viruses emerge every year
 - ▶ Sloppy replication
 - ▶ Constantly evolving
- ▶ Most cause viral syndromes that we never diagnose
- ▶ A mutation that makes a virus more readily transmissible or pathogenic may result in noticeable events
 - ▶ Severe illness, death, anencephaly
- ▶ Then we pick them up and try to learn about them
- ▶ “New RNA viruses, particularly influenza, will continue to cause pandemics, and we must be prepared to deal with them.”

Herbert DuPont MD
Edward H. Kass lecture, IDWeek 2019

Coronaviruses

- ▶ CoV: Single-stranded RNA viruses, 30 Kb (largest known viral RNA)
 - ▶ Capable of genetic recombination if 2 CoV's infect same cell at same time
- ▶ At least 4 HCoV's circulate widely with periodicity, winter seasonality
 - ▶ Mild illnesses in volunteer inoculation studies in 1960's
 - ▶ Reinfection is common, ?due to rapid diminution of antibody levels
- ▶ SARS-CoV: 2002
 - ▶ Fever, HA, malaise/myalgias then 1 week later cough, 25% ARDS
 - ▶ Lymphopenia with normal or sl depressed Neutrophil counts
 - ▶ Elevated CPK, LDH, transaminases, proinflammatory cytokines
- ▶ MERS-CoV: 2012
 - ▶ Similar, plus renal failure

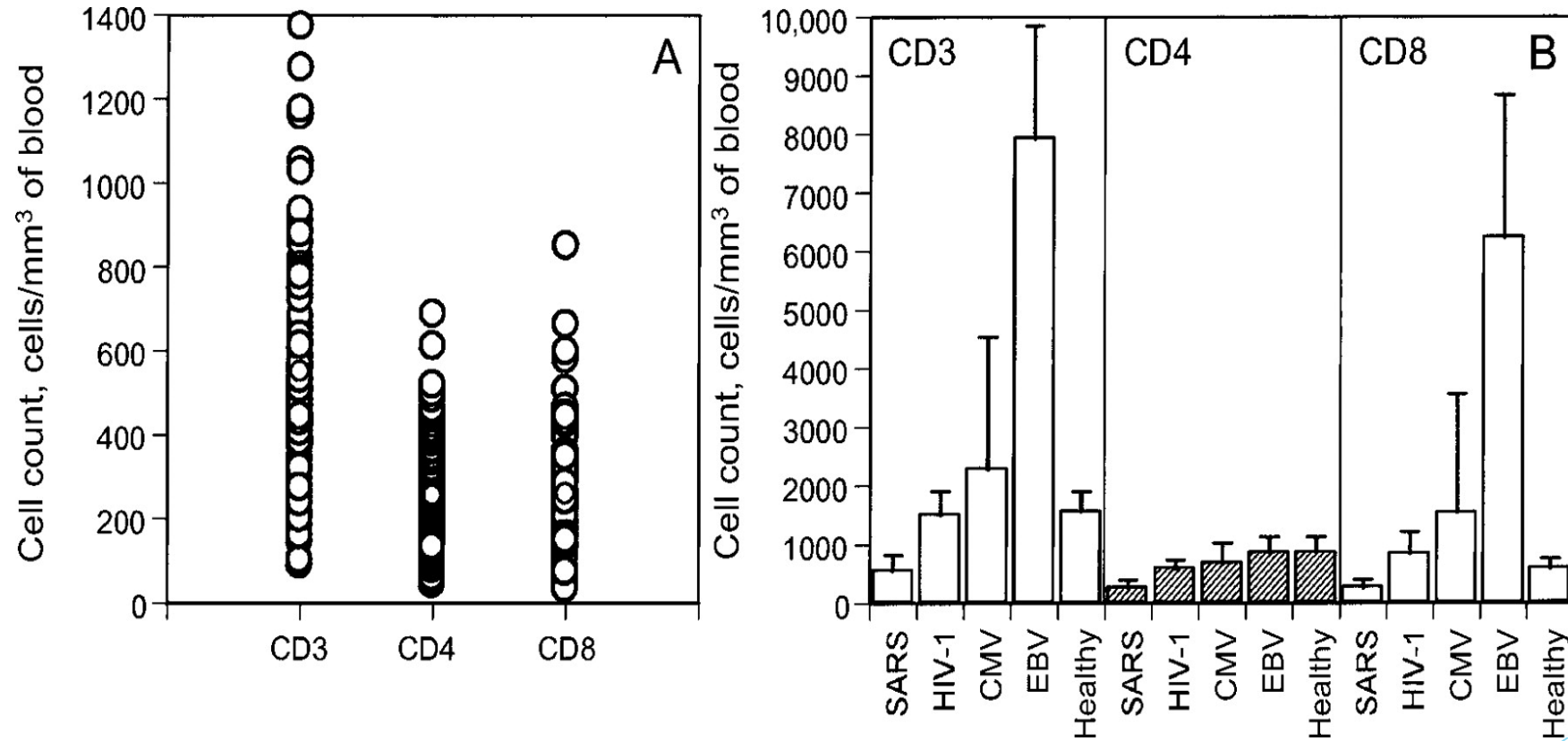
Middle East Respiratory Syndrome Coronavirus Efficiently Infects Human Primary T Lymphocytes and Activates the Extrinsic and Intrinsic Apoptosis Pathways: Chu H, et al, 15 March 2016, JID; 213(6):904-14.

SARS-CoV2 Lab abnormalities

- ▶ Lymphopenia is the most common laboratory finding in COVID-19 and is found in as many as 83% of hospitalized patients.^{1,5}
- ▶ Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase levels, elevated lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater illness severity.^{1,5,6,8,38,55}
- ▶ Elevated D-dimer and lymphopenia have been associated with mortality.^{8,38}
- ▶ Procalcitonin is typically normal on admission but may increase among those admitted to an ICU.⁴⁻⁶
- ▶ Patients with critical illness had high plasma levels of inflammatory makers, suggesting potential immune dysregulation.^{5,56}

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>

Figure 1. Comparison of peripheral changes in CD3, CD4, and CD8 T cell counts in patients who have severe acute respiratory syndrome (SARS) (A) and among healthy individuals and those infected with the SARS virus, HIV-1, cytomegalovirus (CMV), or Epstein-Barr virus (EBV) (B).



J Infect Dis, Volume 189, Issue 4, 15 February 2004, Pages 648-651,

<https://doi.org/10.1086/381535>

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Lymphocyte subsets and cytokines in COVID-19: Chongqing Three Gorges Central Hospital from 26 January to 4 February 2020, n = 123 inpatients diagnosed with COVID-19.

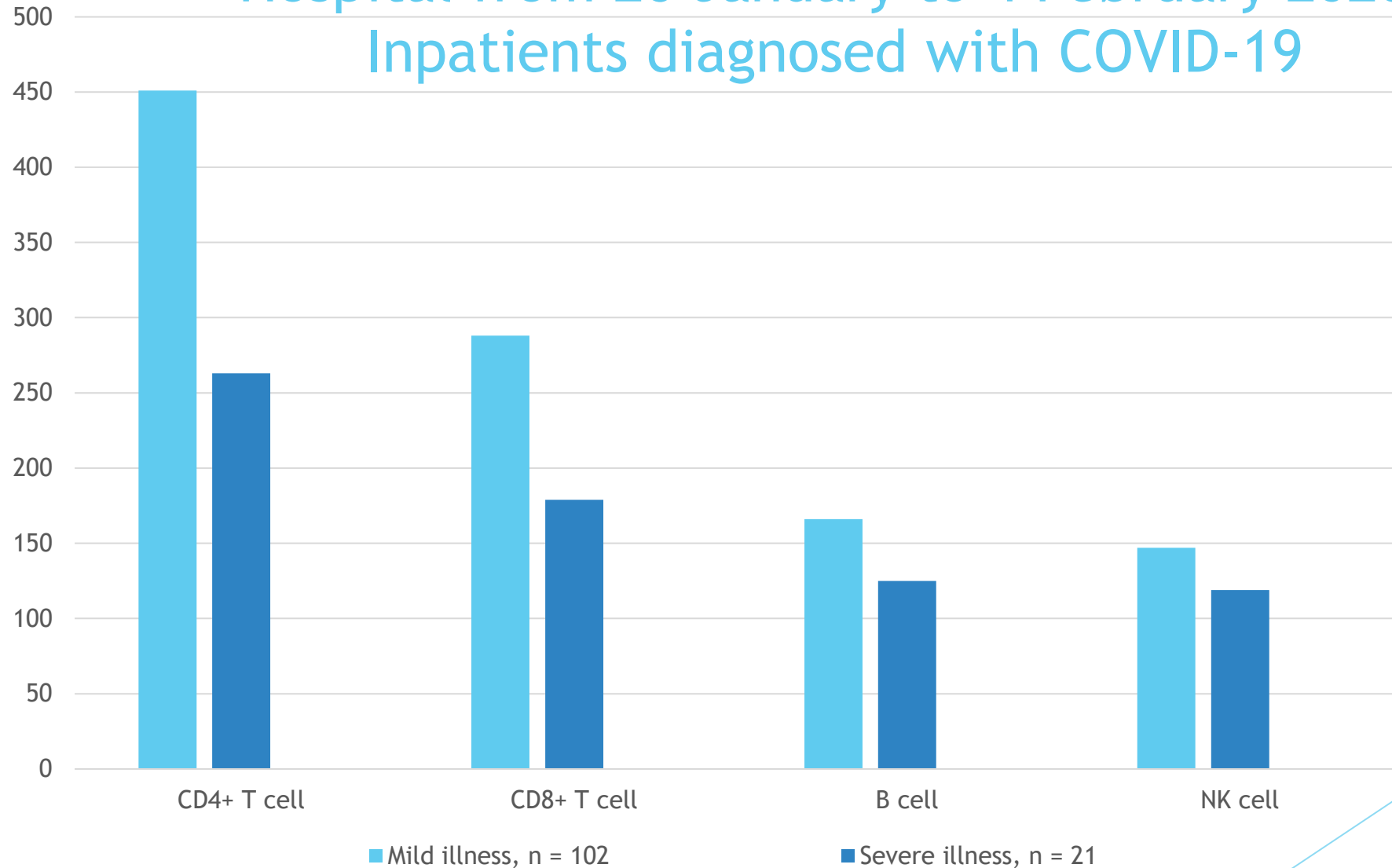
Table 4. Difference analysis of lymphocyte subsets, cytokines and pulmonary inflammatory index between the two groups.

Items	Mild group, <i>n</i> (mean [SD])	Severe group, <i>n</i> (mean [SD])	<i>P</i>
CD4 ⁺ T	102 (451.3 [23.0])	21 (263.2 [28.83])	0.0005
CD8 ⁺ T	102 (288.6 [14.23])	21 (179 [23.87])	0.0013
B cell	102 (166 [11.98])	21 (125.3 [13.49])	0.1375
NK cell	102 (147 [10.36])	21 (119.6 [16.500])	0.258
CD4 ⁺ T/CD8 ⁺ T	102 (1.671 [0.059])	21 (1.509 [0.170])	0.2857
IL-4	102 (1.69 [0.070])	21 (1.83 [0.185])	0.4317
IL-6	45 (13.41 [1.84])	21 (37.77 [7.801])	<0.0001
IL-10	102 (2.464 [0.085])	21 (4.59 [0.378])	<0.0001
IL-17	102 (1.095 [0.0226])	21 (1.16 [0.0571])	0.2463
TNF	102 (4.077 [1.588])	21 (2.948 [0.443])	0.7486
IFN	97 (5.132 [0.841])	21 (6.904 [1.247])	0.3533
PII	102 (0.129 [0.039])	21 (0.508 [0.179])	<0.0001

The normal ranges of: CD4+T = 410-1590, CD8+T = 190-1140, B cell = 90-660, natural killer (NK) cell = 90-590, CD4+T/CD8+T = 0.7 - 2.87

PII = lesion distribution score + lesion size score/total score

Lymphocyte subsets in COVID-19: Chongqing Three Gorges Central Hospital from 26 January to 4 February 2020, Inpatients diagnosed with COVID-19



Wan S, Yi Q, et al British Journal Haematology, 2020; 189: 428

Vaccine strategies

- ▶ Whole, inactivated or attenuated pathogen
 - ▶ Influenza vaccines
- ▶ Subunit approach
 - ▶ Pneumococcal, H flu or Meningococcal capsular antigens
 - ▶ Can conjugate Polysaccharide antigens with a Protein for stronger response
 - ▶ Recombinant “Cut-and-Paste” response
 - ▶ Can insert gene for a target antigen into a less pathogenic virus
 - ▶ mRNA vaccines
- ▶ Phase 1 & 2 trials for safety and dose ranging
- ▶ Phase 3 trials randomized, double-blind, placebo-controlled

SARS-Cov2 vaccines in stage 3 trials: Moderna

- ▶ Moderna mRNA vaccine
 - ▶ Uses mRNA to produce viral proteins
 - ▶ 2 vaccinations 28 days apart
 - ▶ Robust neutralizing antibodies in 45 recipients, appeared safe
 - ▶ Phase 1 per NEJM July 14
 - ▶ Phase 3 trials starting
 - ▶ May need boosting later
- ▶ Enrolling at UCMC, call 513-584-6617 for info
 - ▶ Goal of 500 locally, 30,000 globally

Pfizer/BioNTech/Fosun Pharma

- ▶ mRNA vaccine
- ▶ 2 doses 21 days apart
- ▶ Dose-ranging trial
- ▶ Phase 1 and 2 trial data published in July
 - ▶ 45 subjects developed neutralizing antibodies and T-cell responses

AstraZeneca/Oxford University vaccine

- ▶ Viral vector vaccine
- ▶ Based on a chimpanzee adenovirus called ChAdOx1
- ▶ Phase 1 & 2 results reported in Lancet
 - ▶ 1077 volunteers
 - ▶ Recipients developed good antibody responses
 - ▶ Vaccine was well tolerated
- ▶ Phase 2 & 3 trials underway

CanSinBio vaccine

- ▶ Viral vector vaccine by a Chinese company
- ▶ Based upon Adenovirus ad5
- ▶ Phase 2 results Lancet 20 July

Type	Status	Name	Declined	Enrolled	Local Goal	Global Goal	Brief Description
Interventional			-	-	-	-	-
INPATIENT	ENROLLING	CORONET-1			5	5	Coronavirus Nomacopan Emergency Treatment For COVID 19 Patients With Early Signs Of Respiratory Distress
INPATIENT	CLOSED	Convalescent Plasma (closed)	9	29	100	Expanded Access	Mayo Clinic National Expanded Access Program
INPATIENT	ENROLLING	RUXCOVID-DEVENT	0	3	10	500	Ruxolitinib in Participants With COVID-19–Associated ARDS Who Require Mechanical Ventilation
INPATIENT	ENROLLING	AT-03A-001	0	0	50	180	Study to Evaluate the Safety and Efficacy of AT-527 in Subjects with Moderate COVID-19
INPATIENT	ENROLLING	SCOPE	15	14	30	30	Sirolimus vs placebo
INPATIENT	ENROLLING	LOSARTAN	0	0		220	Losartan to help reduce problems with breathing while recovering from COVID-19
INPATIENT	ENROLLING	MAVRI			15	60	Mavrilimumab to reduce progression of acute respiratory failure in patients with severe COVID-19 pneumonia and systemic hyper-inflammation
INPATIENT	ON-HOLD	DAS181	4	2	10	82	Nebulized anti-viral therapy vs placebo
INPATIENT	START-UP	Rescue 3			10	180	Study to Evaluate the Safety and Efficacy of Razuprotafib in Hospitalized Subjects With Moderate to Severe Coronavirus Disease
INPATIENT	START-UP	ACTIV 1					Inpatient, Phase III Master Protocol Host-targeted Interventions
INPATIENT	START-UP	ACTIV 3					Inpatient, Phase III (2 Stage) Master Protocol Initial Focus: Neutralizing Monoclonal Antibodies
INPATIENT	START-UP	ACTIV 4					Inpatient, Phase III Master Protocol 2 anticoagulants, leading to anticoagulant + antiplatelet, anti-thrombotics combos
INPATIENT	START-UP	TL-895-202			3	146	Cancer COVID-19 study
INPATIENT	CLOSED	ORCHID/PETAL (closed)	9	10	12	510	inpatient Hydroxychloroquine vs placebo
INPATIENT	CLOSED	A5395 (closed)	3	1	40	100	Outpatient Hydroxychloroquine and Azithromycin vs placebo
OUTPATIENT	ENROLLING	CSSC-004	0	1	30	1344	Treatment with Plasma to prevent the progression of infection or lessens the severity of current symptoms in infected patients
OUTPATIENT	ENROLLING	CSSC-001	0	0	15	150	Treatment with Plasma to prevent COVID-19 illness or lessens its severity in exposed patients
OUTPATIENT	ENROLLING	MODERNA VACCINE		21	500	30000	A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine
OUTPATIENT	START-UP	ACTIV 2					Outpatient, Phase II/III Master Protocol Initial Focus: Neutralizing Monoclonal Antibodies
TEST	ENROLLING	RAPID BIOMARKER			200	200	Partnership with Air Force: Support of Rapid, Non-Invasive Biomarker Testing for COVID-19
TEST	ON-HOLD	CATSS			50	510	Clinical Evaluation of the Panbio™ COVID-19 Ag Antigen Test in Symptomatic Subjects (CATSS)
TEST	START-UP	CoVPN 5002			4000	4000	Seroprevalence Survey Study

CHASING THE SUN



What is 24 hours of COVID-19 *Chasing the Sun*?

Kick off **IDWeek** with 24 hours of COVID-19 during *Chasing the Sun*. This global event will begin on Wednesday, Oct. 21 at 10 a.m. ET and conclude on Thursday, Oct. 22 at 10 a.m. ET. **IDWeek** and its partners are joining forces with recognized scientific agencies, non-governmental agencies and infectious diseases organizations from around the world including the Centers for Disease Control and Prevention (CDC), the American Society of Microbiology, Asociación Panamericana de Infectología, the Chinese Society of Infectious Diseases, the European Society of Clinical Microbiology, and the Japanese Association for Infectious Diseases each bringing unique global perspectives and data to cover various aspects of COVID-19 including clinical presentation, treatments, diagnostics, vaccine development, infection control and mitigation strategies and other late breaking issues. Closed captioning in English will be available for this program.

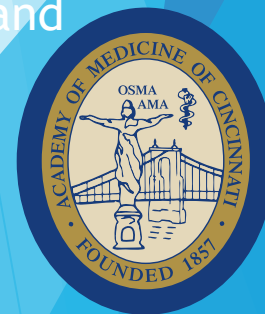


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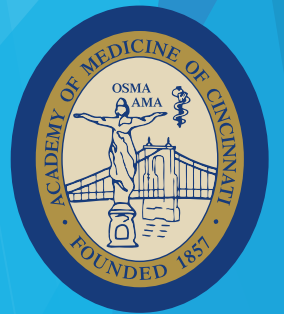
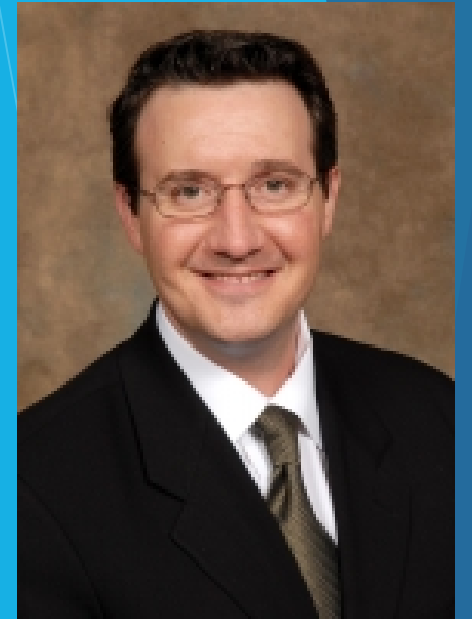
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2020-2021 Academy Council



Installation of Council Members
Matthew Hardin, M.D. - Outgoing President

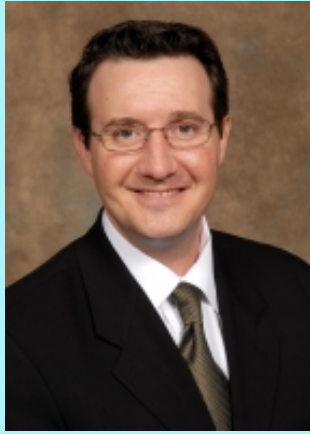




E. Wyman Morriss, MD 2020-2021 President

- ▶ Emergency Medicine, TriHealth
- ▶ AMC councilor 2014-present; AMC Secretary 2018-2019; Finance Committee; Physician Wellness Work Group





Matthew E. Hardin, MD

- ▶ Past President
- ▶ Associate Professor of Internal Medicine and Pediatrics, University of Cincinnati College of Medicine
- ▶ Primary Care Internal Medicine and Pediatrics, UC Health West Chester Campus
- ▶ AMC Executive Committee, 2016 - present; AMC councilor 2013-present; AMC Finance Committee; AMC Social Activities Work Group; and AMC Physician Wellness Work Group



Anne C. Like, MD, MS

- ▶ President-elect
- ▶ Internal Medicine/Occupational Medicine, Independent Practice
- ▶ AMC councilor 2017- present (treasurer 2018, secretary 2019), Chair AMC Physician Wellness Work Group; AMC Finance Committee; Co-chair, Cincinnati Coalition for Physician Wellness; Infection Control Committee, The Christ Hospital Health; Tri-state Occupational Medicine Association.





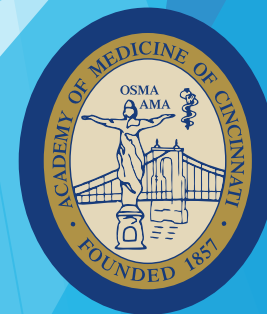
Barry A. Brook, MD

- ▶ Internal Medicine
- ▶ Mercy Health Physicians, Bon Secours Mercy Health
- ▶ Academy Treasurer (2019), AMC councilor 2017-present, AMC Finance Committee, AMC Educational Activities Work Group; Chair, Department of Internal Medicine, Jewish Hospital



Joseph C. Cheng, MD

- ▶ Neurosurgery
- ▶ Frank H. Mayfield Professor and Chair, Department of Neurosurgery, University of Cincinnati College of Medicine
- ▶ UC Health
- ▶ AMC Councilor and Educational Activities Work Group





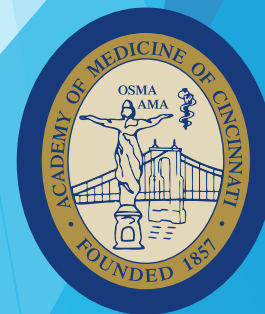
Becky S. McGilligan, MD

- ▶ Internal Medicine
- ▶ McGilligan MD, Inc., on staff The Christ Hospital
- ▶ AMC councilor 2018-present; Social Activities Work Group



Adam G. Miller, MD

- ▶ Orthopaedic Surgery, Foot and Ankle Subspecialist
- ▶ Beacon Orthopaedics and Sports Medicine
- ▶ AMC councilor 2016-present; AMC Physician Wellness Work Group; AMC Social Activities Work Group





Christopher M. Paprzycki, MD

- ▶ Vascular Surgery
- ▶ The Christ Hospital
- ▶ AMC councilor 2018-present; AMC Educational Activities Work Group



Michael R. Schoech, MD

- ▶ Transplant Hepatology
- ▶ UC Health
- ▶ AMC Councilor since 2017 and Educational Activities Work Group





Gregory Kennebeck, MD

- ▶ Internal Medicine
- ▶ UC Health Primary Care
- ▶ AMC Councilor January 2020, appointed to fill an unexpired term
- ▶ AMC Councilor 2020-2023; AMC Physician Wellness Work Group



Kathleen O'Leary, MD, MS

- ▶ Obstetrics/Gynecology & Reproductive Endocrinology Infertility
- ▶ Institute for Reproductive Health
- ▶ AMC Councilor 2020-2023





O'dell Moreno Owens, MD, MPH

- ▶ Reproductive Endocrinology, retired from practice of medicine
- ▶ Interact for Health - President & CEO
- ▶ AMC Councilor 2020-2023



Rebecca Short, MD

- ▶ Dermatology
- ▶ Group Health, TriHealth Physician Partners
- ▶ AMC Councilor 2020-2023



2020-2021 Academy Council

President E. Wyman Morriss, MD (TriHealth)

Past President Matthew E. Hardin, MD (UC Health)

President-elect Anne C. Like, MD (The Christ Hospital)



Councilors

Barry A. Brook, MD (Mercy Health) • Joseph Cheng, MD (UC Health)

Gregory Kennebeck, MD (UC Health)

Becky S. McGilligan, MD (McGilligan MD, Inc.)

Adam G. Miller, MD (Beacon Orthopaedics & Sports Medicine)

Kathleen O'Leary, MD (Institute for Reproductive Health)

O'dell M. Owens, MD (Interact for Health)

Chris M. Paprzycki, MD (The Christ Hospital)

Michael R. Schoech, MD (UC Health) • Rebecca Short, MD (TriHealth)



Outgoing Council Members

Thank you for your service

- ▶ Carol L. Egner, who has served on the Academy of Medicine Council since 2013, President 2018-2019

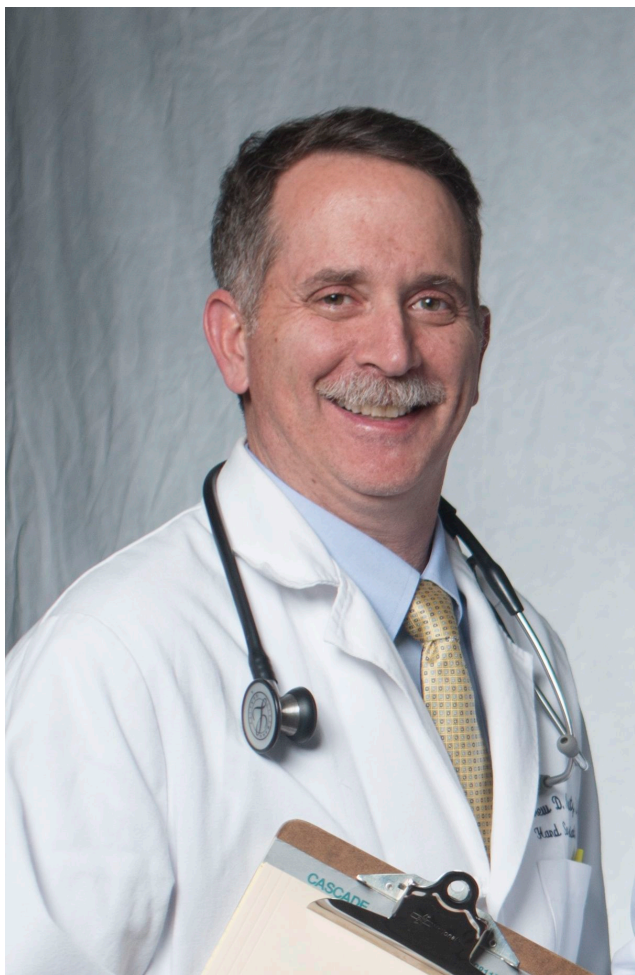


- ▶ Haleem N. Chaudhary, MD, who served as an Academy Councilor from 2017-2020



- ▶ Lisa A. Haglund, MD, who served as an Academy Councilor from 2014-2020





Presentation of the Academy Foundation 2020 UC Medical Student Scholarship

Presented by Academy
Foundation President
Andrew Markiewitz, MD

Molly O'Shea

2020 Academy Foundation Medical
Student Scholarship Recipient

- Fourth-year Medical Student,
University of Cincinnati College
of Medicine
- BS, Neuroscience, The Ohio
State University, 2015
- Research Intern, Urban Health
Project, UCCM & Project
Connect



COVID-19: Q & A

Moderated by Dr. Hardin & Dr. Morriss



Stephen P. Blatt, MD, FACP
TriHealth

- Medical Director for Infectious Diseases
- System Chief for Medical Specialties



Dheeraj Goyal, MD, MPH
Mercy Fairfield Hospital

- Medical Director, Department of Infectious Diseases
- Chair, Infection Control and Antibiotic Stewardship Committees



Thomas Lamarre, Jr., MD
The Christ Hospital Physicians

- Medical Director of Infectious Diseases
The Christ Hospital Network



Lisa Haglund, MD, FACP, FIDSA
University of Cincinnati

- Associate Professor of Clinical Medicine
UC Division of Infectious Diseases

Guests: If you would like to submit a question, use the GoToMeeting Question tab



Thank you for joining us this evening

We hope to see you at the upcoming Academy Golf Outing on September 28 and the Annual Meeting Awards Celebration on March 3 at the Cincinnati Art Museum.

We look forward to a new and exciting year at the Academy of Medicine of Cincinnati.

All registrants will receive a copy of this slide deck
If you want a copy of this video, email npeterson@academyofmedicine.org

