COVID-19: Public Health and Scientific Challenges

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Viewpoint

Coronavirus Infections—More Than Just the Common Cold

CI Paules, HD Marston and AS Fauci
Coronavirus Phylogenetic Tree

Human coronaviruses

Source: SM Gygi, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.
Coronavirus Phylogenetic Tree

Human coronaviruses

Source: SM Gygi, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.
Severe Human Coronavirus Disease: Past as Prologue


Middle East Respiratory Syndrome (MERS) (2012–present)
Novel Human Virus? Pneumonia Cases Linked to Seafood Market in China Stir Concern

By Dennis Normile

China Identifies New Strain of Coronavirus as Source of Pneumonia Outbreak
Coronavirus Phylogenetic Tree

Human coronaviruses

0.1

Figure courtesy of S.M. Gygli, Ph.D., NIAID. Based on 440 bp nucleotide sequences of RNA dependent RNA polymerase (RdRp).
**Coronavirus Disease 2019 (COVID-19)**

- **COVID-19** is the disease caused by the novel coronavirus **SARS-CoV-2**
COVID-19 Globally

39.9 million cases
1,113,464 deaths

Sources: NPR.org; Worldometer. Data as of 10/17/2020
COVID-19 in the United States

8.0 million cases
217,918 deaths

Cases/100,000
- 0-701
- 929-1,593
- 1,707-2,178
- 2,236-2,667
- 2,831-3,326
- 3,470-4,113

Source: CDC. Data as of 10/17/2020.
United States vs. Europe
New COVID-19 Cases: US vs. EU

7-day rolling average of new COVID-19 cases, January 1 to October 17, 2020

Source: Our World in Data
Change in Mobility Over Time: Parks and Outdoor Spaces

Source: Our World in Data
Change in Mobility Over Time: Workplaces

Source: Our World in Data
Change in Mobility Over Time: Grocery and Pharmacy Stores

Source: Our World in Data
Virology
**SARS-CoV-2 Virology**

- **Beta-CoV:** same subgenus as SARS CoV-1 and some bat CoVs
- **RNA virus:** enveloped, positive-sense, single-stranded
- **Large genome:** ~30,000 Kb
- **4 structural proteins:** S, E, M, N
  - S allows virus to attach to and fuse with cell membrane
- **ACE2 receptor:** cell receptor

Images: Florian Krammer; NIAID VRC
Transmission
SARS-CoV-2 Transmission

- Mainly through exposure to respiratory droplets when close (≤6 ft) to an infected person.

- Sometimes through droplets or particles that remain in the air (aerosols) over time and various distances (> or ≤6 ft).

- Less commonly through contact with contaminated surfaces.

- Virus found in stool, blood, semen and ocular secretions; role in transmission unknown.
Risk of Transmission

- Varies by type and duration of exposure, prevention measures used, and individual factors (e.g., viral load)

- Transmissions most common among household contacts, in congregate or health care settings when PPE not used, and in closed settings (e.g., cruise ships, nursing homes, prisons)

- Factors that may increase the risk of airborne transmission include:
  - Crowded, enclosed spaces with poor ventilation
  - Singing, speaking loudly, or breathing heavily
High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice — Skagit County, Washington, March 2020

L Hamner, H Leibrand et al.
Community Transmission of SARS-CoV-2 at Two Family Gatherings — Chicago, Illinois, February–March 2020
I Ghiai, JE Layden et al.

High COVID-19 Attack Rate Among Attendees at Events at a Church — Arkansas, March 2020
A James, H Kirking et al.
Community Exposures among Symptomatic Adults – 11 U.S. Healthcare Facilities

Adjusted Odds Ratio

Shopping
Restaurant
Office setting
Salon
Home, more than 10
Gym
Public transportation
Bar/coffee shop
Church/religious gathering

Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review

Data from 16 cohorts, total n= 45,000+

Asymptomatic persons account for ~40-45% of SARS-CoV-2 infections
The Implications of Silent Transmission for the Control of COVID-19 Outbreaks

SM Moghadas, AP Galvani et al.

Modeling study estimates that individuals without symptoms account for >50% of transmission
Fundamentals to Prevent Acquiring and Transmitting SARS-CoV-2

- Universal wearing of masks/cloth face coverings
- Maintain physical distance – at least 6 feet
- Avoid crowds and congregate settings
- Outdoors better than indoors
- Frequent washing of hands
Clinical Manifestations
# COVID-19 Clinical Presentation

- **Fever**: 83–99%
- **Cough**: 59–82
- **Fatigue**: 44–70
- **Anorexia**: 40–84
- **Shortness of breath**: 31–40
- **Myalgias**: 11–35

**Other non-specific symptoms reported**
- Sore throat, nasal congestion, headache, diarrhea, nausea, vomiting. Loss of smell/taste preceding the onset of respiratory symptoms.

Source: WHO, 5/2020
Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China

- Mild/Mod: 81%
- Severe: 14%
- Critical: 5%

Case-fatality rate: 2.3%

### Manifestations of Severe COVID-19

- Neurological disorders
- Hyperinflammation
- Acute respiratory distress syndrome (ARDS)
- Cardiac dysfunction
- Hypercoagulability
- Acute kidney injury
- Multisystem inflammatory syndrome in children (MIS-C)
Post-COVID-19 Syndrome

From ‘Brain Fog’ to Heart Damage, COVID-19’s Lingering Problems Alarm Scientists
J Couzin-Frankel

Long After the Fire of a COVID-19 Infection, Mental and Neurological Effects Can Still Smolder
E Cooney
People at Increased Risk for Severe COVID-19 Illness

- Older adults
- People of any age with certain underlying medical conditions

Source: CDC, 6/25/2020
People at Increased Risk for Severe COVID-19 Illness

- Older adults

- People of any age with certain underlying medical conditions

Source: CDC, 6/25/2020
Cumulative Rates of Laboratory-Confirmed COVID-19-Associated Hospitalizations by Age, United States, March 1 – October 10, 2020

Source: CDC COVID-NET. Data from 14 states.
People at Increased Risk for Severe COVID-19 Illness

- Older adults

- People of any age with certain underlying medical conditions

Source: CDC, 6/25/2020
Underlying Medical Conditions Associated with Increased Risk for Severe COVID-19 Illness

- Cancer
- Chronic kidney disease
- Chronic obstructive pulmonary disease (COPD)
- Diabetes, type 2
- Heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)
- Immunocompromised state from solid organ transplant
- Obesity (BMI ≥ 30)
- Sickle cell disease
- Smoking

Source: CDC, 10/6/2020
Underlying Medical Conditions That May Confer Increased Risk for Severe COVID-19 Illness

- Asthma (moderate-to-severe)
- Cerebrovascular disease
- Cystic fibrosis
- Diabetes, type 1
- Hypertension
- Immunocompromised state from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids or other immune-weakening medicines
- Neurologic conditions (e.g. dementia)
- Liver disease
- Overweight (BMI > 25 but < 30)
- Pregnancy
- Pulmonary fibrosis
- Thalassemia

Source: CDC, 10/6/2020
More Than 40% Of U.S. Adults Are Susceptible To Severe COVID-19

Prevalence of underlying conditions in U.S. adults in 2018

- Any underlying condition: 40.7%
- Obesity*: 30.9%
- Diabetes mellitus: 11.4%
- COPD: 6.9%
- Heart disease: 6.8%
- Chronic kidney disease: 3.1%

*BMI ≥ 30kg/m²

Source: H Razzaghi et al., MMWR Vol. 69, July 24, 2020
Viewpoint

COVID-19 and Racial/Ethnic Disparities

MW Hooper, AM Nápoles and EJ Pérez-Stable

“The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations.”
Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – October 10, 2020

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Rate per 100,000 population</th>
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<td>Hispanic/Latino</td>
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<tr>
<td>American Indian/Alaska Native</td>
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<td>Black, Non-Hispanic</td>
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<td>Asian/Pacific Islander</td>
<td>114</td>
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<tr>
<td>White, Non-Hispanic</td>
<td>86</td>
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Source: CDC COVID-NET. Data from 14 states.
Therapeutics
Expert U.S. Panel Develops NIH Treatment Guidelines for COVID-19

“Living document” expected to be updated often as new clinical data accrue

Covid19treatmentguidelines.nih.gov
Therapeutics for COVID-19

Recommended by the NIH COVID-19 Treatment Guidelines Panel for Certain Patients
- Remdesivir (investigational antiviral)
- Dexamethasone (corticosteroid)

Examples of Other Investigational Therapies
- Antivirals
- Blood-derived products, e.g., convalescent plasma, hyperimmune globulin
- Monoclonal antibodies against SARS-CoV-2
- Immunomodulators, e.g., cytokine inhibitors, interferons
- Adjunct therapies, e.g., anticoagulants
JH Beigel, HC Lane et al. for the ACTT-1 Study Group Members

- Hospitalized patients on remdesivir recovered more quickly than those on placebo (median 10 days vs 15 days, P<0.001)

- A trend toward decreased mortality: hazard ratio = 0.73 (95% CI: 0.52–1.03)

- 1,062 patients from 10 countries: U.S., Europe and Asia
Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report

The RECOVERY Collaborative Group

- RECOVERY trial in UK -- 6,425 patients randomized to receive dexamethasone 6 mg once per day (oral or IV) for up to ten days or usual care alone

- Dexamethasone reduced 28-day mortality by 36% in ventilated patients and by 18% in other patients receiving oxygen

- No benefit for patients not receiving respiratory support
Vaccines
Unprecedented collaboration and resources will be required to research and develop safe and effective vaccines for COVID-19 that can be manufactured and delivered in the scale of billions of doses to people globally.
# Selected COVID-19 Vaccine Candidates

<table>
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<tr>
<th>Platform</th>
<th>Developer</th>
<th>Phase 1/2</th>
<th>Phase 2/3</th>
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Just 50% of Americans Plan to Get a COVID-19 Vaccine. Here’s How to Win Over the Rest

W Cornwall

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<td>Overall</td>
<td>49%</td>
<td>31%</td>
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<td>Age 60 and older</td>
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<td>Hispanic</td>
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Do you plan to get a coronavirus vaccine when one is available?