COVID-19: Public Health and Scientific Challenges

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September 30, 2020

Disclosures

- No relevant financial relationships with commercial interests

Viewpoint

Coronavirus Infections—More Than Just the Common Cold

Cl Paulus, HD Marston and AS Fauci

Coronavirus Phylogenetic Tree

Severe Human Coronavirus Disease: Past as Prologue

Middle East Respiratory Syndrome (MERS) (2012–present)
Coronavirus Disease 2019 (COVID-19)

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

COVID-19 Globally

United States vs. Europe
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 Kbp
- 4 structural proteins: S, E, M, N
  - S allows virus to attach to and fuse with cell membrane
- ACE2 receptor: cell receptor

Change in Mobility Over Time: Parks and Outdoor Spaces
- Italy
- United States
- Spain

Change in Mobility Over Time: Grocery and Pharmacy Stores
- Spain
- United States
- Italy

Change in Mobility Over Time: Workplaces
- Italy
- Spain
- United States

New COVID-19 Cases: US vs. EU
- 7-day rolling average of new COVID-19 cases, January 1 to September 29, 2020
- United States
- European Union
Transmission

- Transmission between people in close contact
- Transmission via particles that remain in the air over time and distance
- Infected surfaces
- Virus found in stool, blood, semen and ocular secretions; role in transmission unknown
- Animals (including domesticated) not major source of human infection

Risk of Transmission

- Varies by the type and duration of exposure, use of preventive measures, and individual factors (e.g., the amount of virus in respiratory secretions)
- Secondary infections most common among household contacts, in congregate or health care settings when personal protective equipment not used, and in closed settings (e.g., cruise ships)
- Numerous clusters of cases after social or work gatherings highlight the risk of transmission through close, non-household contact
High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice — Skagit County, Washington, March 2020

Community Exposures among Symptomatic Adults — 11 U.S. Healthcare Facilities

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

The Implications of Silent Transmission for the Control of COVID-19 Outbreaks

Fundamentals for Prevention of Acquisition and Transmission of SARS-CoV-2
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.

Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China

- Mild/Mod 81%
- Severe 14%
- Critical 6%

Case-fatality rate: 2.3%

Manifestations of Severe COVID-19 Disease

- Acute respiratory distress syndrome (ARDS)
- Hyperinflammation
- Acute cardiac injury, arrhythmias, cardiomyopathy
- Acute kidney injury
- Neurological disorders
- Hypercoagulability leading to thromboembolic complications, including pulmonary embolism and acute stroke
- Multisystem inflammatory syndrome in children (MIS-C)

COVID “Long-Haulers”
Collateral Negative Effects of COVID-19 on Other Health Issues

Changes in the Number of US Patients With Newly Identified Cancer Before and During the Coronavirus Disease 2019 (COVID-19) Pandemic

COVID-19 and Cancer

People at Increased Risk for Severe COVID-19 Illness

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

CDC Morbidity and Mortality Weekly Report (MMWR)

Potential Indirect Effects of the COVID-19 Pandemic on Use of Emergency Departments for Acute Life-Threatening Conditions — United States, January–May 2020

JAMA

COVID-19 Pandemic Ongoing Impact on the Cancer Community: May 2020

- 17% of patients in active treatment who reported delays to their cancer therapy
- 67% of cancer patients and survivors expressed concern about health as shelter in place orders lifted

Science

COVID-19-related reductions in cancer screening and treatment over the next decade could result in 10,000 excess deaths from breast and colorectal cancer

Beyond clinical care, the COVID-19 pandemic has caused an unprecedented disruption throughout the cancer research community, shuttering many labs and slowing down cancer clinical trial operations
People at Increased Risk for Severe COVID-19 Illness

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

Cumulative Rates of Laboratory-Confirmed COVID-19-Associated Hospitalizations by Age, United States, March 1 – September 19, 2020

Underlying Medical Conditions That May Confer Increased Risk for Severe COVID-19 Illness

- Asthma
- Other chronic lung diseases
- Cerebrovascular disease
- Diabetes, type 1
- Hypertension
- Immunosuppressed state from bone marrow transplant, immune deficiencies, HIV, use of corticosteroids or other immunosuppressive medications

- Inherited metabolic disorders
- Neurologic conditions
- Liver disease
- Pregnancy
- Smoking
- Thalassemia

Underlying Medical Conditions Strongly Associated with Increased Risk for Severe COVID-19 Illness

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

COVID-19 and Racial/Ethnic Disparities

"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 – September 19, 2020

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Hospitalization Rate per 100,000 population</th>
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<tbody>
<tr>
<td>Hispanic/Latino</td>
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<tr>
<td>Black, Non-Hispanic</td>
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<tr>
<td>American Indian, Alaska Native</td>
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<tr>
<td>Asian, Pacific Islander</td>
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<tr>
<td>White, Non-Hispanic</td>
<td>78</td>
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Source: CDC COVID-19 Data from iCares

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**Therapeutics**

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**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
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

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Monoclonal Antibody Studies in COVID-19

- Outpatient
- Inpatient
- Family prophylaxis
- Nursing home prophylaxis

Vaccines

Selected COVID-19 Vaccine Candidates

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<th>Platform</th>
<th>Developer</th>
<th>Phase 1/2</th>
<th>Phase 2/3</th>
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When will we return to normal?

Prevention of COVID-19 in the Absence of a Vaccine

Prevention of COVID-19 with a Moderately Effective Vaccine and Moderate Uptake

Prevention of COVID-19 with a Highly Effective Vaccine and Widespread Uptake

COVID-19 Prevention Network

coronaviruspreventionnetwork.org