COVID-19 and the Research Response

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
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Coronavirus Phylogenetic Tree

Human coronaviruses

Severe Human Coronavirus Disease: Past as Prologue

Severe Acute Respiratory Syndrome (SARS) (2002-2003)
Middle East Respiratory Syndrome (MERS) (2012-present)

Coronavirus Phylogenetic Tree

Human coronaviruses

China Identifies New Strain of Coronavirus as Source of Pneumonia Outbreak

Novel Human Virus? Pneumonia Cases Linked to Seafood Market in China Stir Concern
By Dennis Normile

Science

The Washington Post

Published online January 30, 2020

Viewpoint
Coronavirus Infections—More Than Just the Common Cold
CI Paulus, HD Marston and AS Fauci

AS Fauci/NIAID
Coronavirus Phylogenetic Tree

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

COVID-19 Globally: 18.9 Million Cases in 215 Countries and Territories

Reported COVID-19 Cases and Deaths in the United States

New COVID-19 Cases: US vs. EU

New COVID-19 Cases by Region, United States, March 1 – August 4, 2020
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

SARS-CoV-2 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

COVID-19 Clinical Presentation
- Data from 16 cohorts, total n = 45,000+
- Asymptomatic persons account for ~40-45% of SARS-CoV-2 infections
- 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.

COVID-19: Wide Spectrum of Disease
- Asymptomatic Illness: No symptoms
- Mild Illness: Uncomplicated upper respiratory tract infection
- Moderate Disease: Pneumonia without the need for supplemental oxygen
- Severe Pneumonia: Pneumonia plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 < 90% on room air
- Critical Illness: ARDS, sepsis, septic shock, multiple organ dysfunction/failure

Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China
- Case-fatality rate: 2.3%
- Mild/Mod: 81%
- Severe: 14%
- Critical: 5%

**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)

**Numerous Non-Pulmonary Complications of COVID-19 Have Been Reported**
- Neurological disorders
- Hyperinflammation
- Cardiac dysfunction
- Hypercoagulability
- Acute kidney injury
- Multisystem inflammatory syndrome in children (MIS-C)

**People at Increased Risk for Severe COVID-19 Illness**
- Older adults
- People of any age with certain underlying medical conditions

**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
- Immunocompromised state from solid organ transplant

**Underlying Medical Conditions That May Confer Increased Risk for Severe COVID-19 Illness**
- Asthma
- Other chronic lung diseases
- Cerebrovascular disease
- Diabetes, type 1
- Hypertension
- Immunocompromised 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

**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 – July 25, 2020

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<tr>
<th>Race/Ethnicity</th>
<th>Rate per 100,000 population</th>
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<td>American Indian/Alaska Native</td>
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<tr>
<td>Hispanic/Latino</td>
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<td>Black, Non-Hispanic</td>
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<td>Asian</td>
<td>73</td>
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<tr>
<td>White, Non-Hispanic</td>
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</table>

Source: CDC COVID-19 Data from 14 states.

Nationwide, Black People are Dying at 2.5 Times the Rate of White People

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<th>Race/Ethnicity</th>
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<td>Pacific Islander</td>
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<td>Two or more races</td>
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Tests for SARS-CoV-2

Molecular tests detect genetic material from virus
Antigen tests detect proteins from virus
Antibody tests detect proteins in blood made in response to infection with virus

Adapted from San Diego Union Tribune

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 therspies, e.g., anticoagulants

Remdesivir for the Treatment of Covid-19 — Preliminary Report

- JH Boul, HC Lane et al. for the ACTT-1 Study Group Members
- Patients who received remdesivir had a 32% faster time to recovery than those who received placebo (p<0.001)
- Results also suggested a survival benefit
- N=1,063 patients from 10 countries in U.S., Europe, Asia
**COVID-19 Prevention: Personal Preventive Measures**

- Diligent hand washing
- Avoiding close contact
  - Avoiding crowds/mass gatherings
  - Physical distancing, >6 feet
- Covering mouth and nose with mask/cloth face cover
- Covering sneezes/coughs
- Avoiding face-touching
- Regular cleaning/disinfecting of frequently touched objects

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**COVID-19 Prevention: Public Health Measures**

- Social/physical distancing orders
- Stay-at-home orders
- School, venue, and nonessential business closure
- Bans on public gatherings
- Travel restriction with exit and/or entry screening
- Aggressive case identification and isolation
- Contact tracing and quarantine

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**Enacting National Social Distancing Policies Corresponds With Dramatic Reduction in COVID-19 Infection Rates**

Social distancing policies enacted nationally in 46 countries
- Prevented ~1.57M cases of COVID-19 over 2 weeks, representing a 65% decrease in new cases

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**A Strategic Approach to COVID-19 Vaccine R&D**

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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<th>Platform</th>
<th>Developer</th>
<th>Phase 1/2</th>
<th>Phase 2/3</th>
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<td>BIONTECH</td>
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**COVID-19 Prevention Network**

[coronaviruspreventionnetwork.org](http://coronaviruspreventionnetwork.org)