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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Disclosures

- No relevant financial relationships with commercial interests
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
Global Spread of COVID-19 – Jan. 10, 2020

Total cases: 41

Number of cases:
- 1-99
- 100-999
- 1,000-9,999
- 10,000-99,999
- 100,000-999,999
- ≥1,000,000

Source: Johns Hopkins University
Global Spread of COVID-19 – Mar. 30, 2020

Total cases: 783,037

Source: Johns Hopkins University
Global Spread of COVID-19 – Apr. 30, 2020

Total cases: 3.3 million

Source: Johns Hopkins University
Global Spread of COVID-19 – May 10, 2020

Total cases: 4.1 million

Source: Johns Hopkins University
Global Spread of COVID-19 – May 20, 2020

Total cases: 5.0 million

Source: Johns Hopkins University
Global Spread of COVID-19 – June 10, 2020

Total cases: 7.4 million

Number of cases
- 1-99
- 100-999
- 1,000-9,999
- 10,000-99,999
- 100,000-999,999
- ≥1,000,000

Source: Johns Hopkins University
Total cases: 8.8 million
Global Spread of COVID-19 – June 30, 2020

Total cases: 10.5 million

Source: Johns Hopkins University
COVID-19 Globally: 11.3 Million Cases in 215 Countries and Territories

11.3 million cases
530,551 deaths

Sources: NPR.org; Worldometer. Data as of 7/5/2020, 12:00 pm.
Viewpoint

Coronavirus Infections—More Than Just the Common Cold

CI Paules, HD Marston and AS Fauci
Basic Biology
Coronavirus Phylogenetic Tree

Human coronaviruses

Figure courtesy of S.M. Gygli, Ph.D., NIAID. Based on 440 bp nucleotide sequences of RNA dependent RNA polymerase (RdRp).
Coronavirus Phylogenetic Tree

Human coronaviruses

Figure courtesy of S.M. Gygli, Ph.D., NIAID. Based on 440 bp nucleotide sequences of RNA dependent RNA polymerase (RdRp).
**SARS-CoV-2 Virology**

- **Beta coronavirus** in the same subgenus as the SARS virus and several bat coronaviruses
- Enveloped, positive-sense single-stranded RNA (+ssRNA) virus
- Large genome: ~30,000 kilobases
- 4 structural proteins: S, E, M, N
- **S protein** allows virus to attach to and fuse with membrane of host cell
- **ACE2** is cellular receptor

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

- Person-to-person transmission (<6 feet) via respiratory droplets (>5µm diameter)
- Aerosols: <5µm 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
Prevalence of Asymptomatic SARS-CoV-2 Infection
A Narrative Review
DP Oran and EJ Topol

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

Y Bai, M Wang et al.

A Familial Cluster of Infection Associated With the 2019 Novel Coronavirus Indicating Possible Person-to-Person Transmission During the Incubation Period

P Yu, Y Han et al.
Clinical Manifestations
Median COVID-19 Incubation Period is 4-5 Days (Range: 2-14 Days)

Sources: CDC; Lauer, Ann Intern Med 2020; Xu, BMJ 2020; Guan NEJM 2020
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
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic Illness</td>
<td>No symptoms</td>
</tr>
<tr>
<td>Mild Illness</td>
<td>Uncomplicated upper respiratory tract infection</td>
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<tr>
<td>Moderate Disease</td>
<td>Pneumonia without the need for supplemental oxygen</td>
</tr>
<tr>
<td>Severe Pneumonia</td>
<td>Pneumonia plus one of the following: respiratory rate &gt; 30 breaths/min; severe respiratory distress; or SpO2 &lt; 90% on room air</td>
</tr>
<tr>
<td>Critical Illness</td>
<td>ARDS, sepsis, septic shock, multiple organ dysfunction/failure</td>
</tr>
</tbody>
</table>

Sources: CDC, WHO
Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China

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

Case-fatality rate: 2.3%

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 Strongly Associated with Increased Risk for Severe COVID-19 Illness

- Chronic kidney disease
- Chronic Obstructive Pulmonary Disease (COPD)
- Immunocompromised state from solid organ transplant
- Obesity (BMI ≥ 30)
- Serious heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)
- Sickle cell disease
- Type 2 diabetes mellitus

Source: CDC, 6/25/2020
<table>
<thead>
<tr>
<th>Medical Conditions</th>
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</thead>
<tbody>
<tr>
<td>Asthma</td>
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<td>Cerebrovascular disease</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Pregnancy</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Use of corticosteroids or other immunosuppressive</td>
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<tr>
<td>medications</td>
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<tr>
<td>Bone marrow transplantation</td>
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<tr>
<td>HIV</td>
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<tr>
<td>Immune deficiencies</td>
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<tr>
<td>Inherited metabolic disorders</td>
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<tr>
<td>Neurologic conditions</td>
</tr>
<tr>
<td>Other chronic lung diseases</td>
</tr>
<tr>
<td>Liver disease</td>
</tr>
<tr>
<td>Type 1 diabetes mellitus</td>
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<tr>
<td>Thalassemia</td>
</tr>
</tbody>
</table>

Source: CDC, 6/25/2020
Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – June 27, 2020

- American Indian/Alaska Native: 261
- Black, Non-Hispanic: 213
- Hispanic/Latino: 205
- Asian/Pacific Islander: 58
- White, Non-Hispanic: 46

Rate per 100,000 population

Source: CDC COVID-NET. Data from 14 states.
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)
Therapeutics
Investigational Therapeutics for COVID-19

- Remdesivir
- Other broad-spectrum antivirals
- Convalescent plasma/hyperimmune immunoglobulin
- Repurposed drugs, e.g. hydroxychloroquine, lopinavir/ritonavir
- Host modifiers/immune-based therapies
- Anti-SARS-CoV-2 monoclonal antibodies
- Others
Remdesivir for the Treatment of Covid-19 — Preliminary Report

JH Beigel, 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
Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report

P Horby et al. and 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 35% in ventilated patients and by 20% in other patients receiving oxygen

No benefit among those patients who did not require respiratory support
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
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.
<table>
<thead>
<tr>
<th>Platform</th>
<th>Developer</th>
<th>Phase 1/2</th>
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<td>Nucleic acid</td>
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<td><strong>gsk SANOFI</strong></td>
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