

COVID-19 and the Research Response

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1



Viewpoint

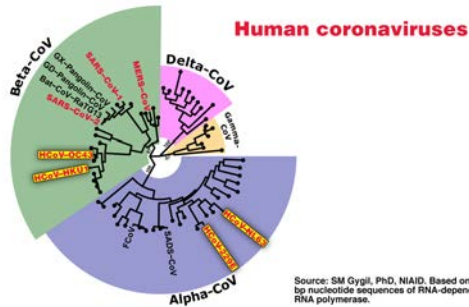
Coronavirus Infections—More Than Just the Common Cold

CI Paules, HD Marston and AS Fauci

AS Fauci/NIAID

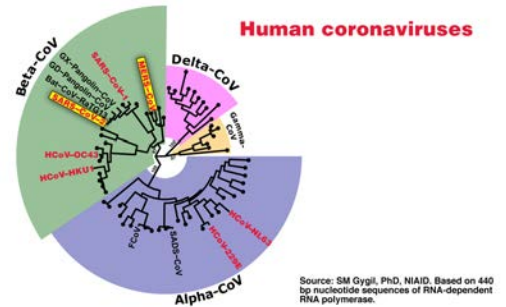
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Coronavirus Phylogenetic Tree



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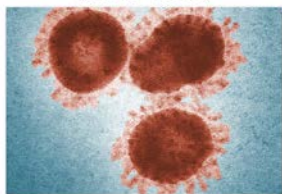
Coronavirus Phylogenetic Tree



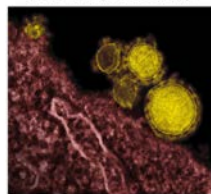
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Severe Human Coronavirus Disease: Past as Prologue

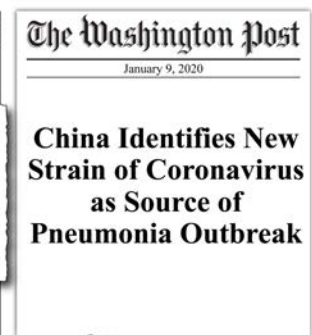
Severe Acute Respiratory Syndrome (SARS) (2002–2003)



Middle East Respiratory Syndrome (MERS) (2012–present)

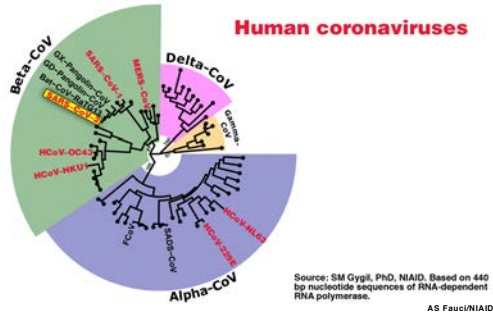


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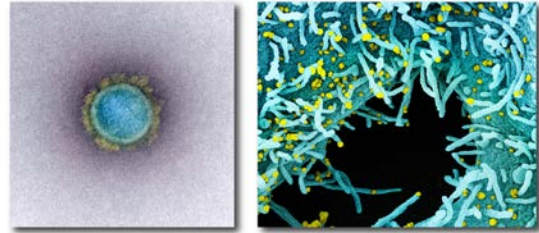
Coronavirus Phylogenetic Tree



7

Coronavirus Disease 2019 (COVID-19)

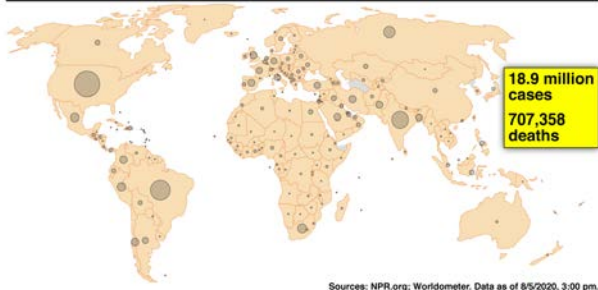
■ **COVID-19** is the disease caused by the novel coronavirus **SARS-CoV-2**



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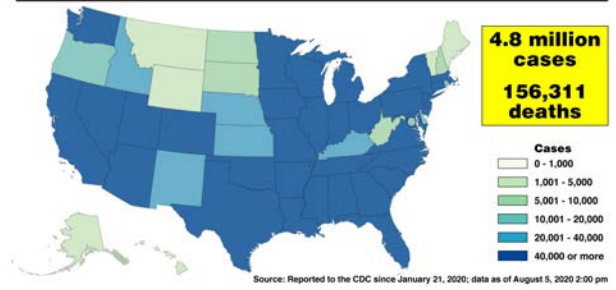
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COVID-19 Globally: 18.9 Million Cases in 215 Countries and Territories



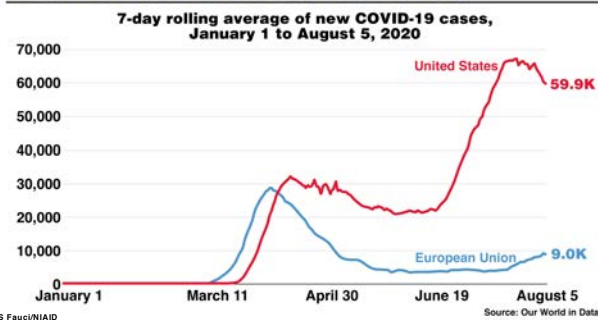
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Reported COVID-19 Cases and Deaths in the United States



10

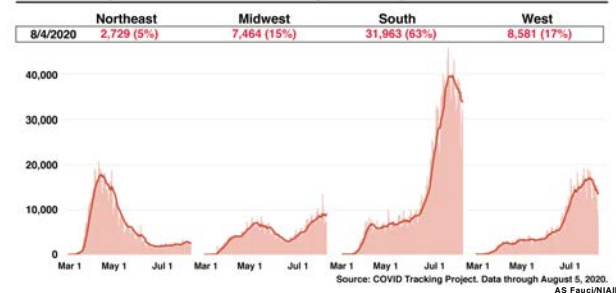
New COVID-19 Cases: US vs. EU



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11

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

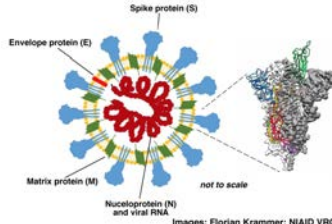


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SARS-CoV-2 Virology

- **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

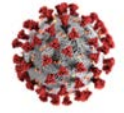


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13

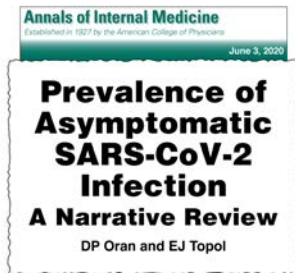
SARS-CoV-2 Transmission

- 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



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14



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

- Asymptomatic persons account for ~40-45% of SARS-CoV-2 infections

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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

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16

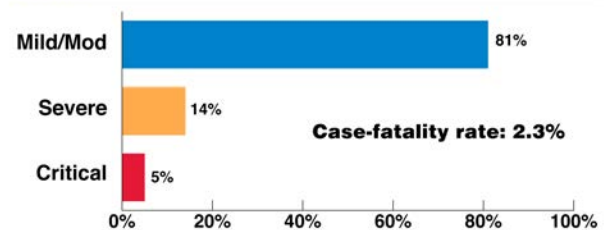
COVID-19: Wide Spectrum of Disease

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

Sources: CDC, WHO
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17

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

Source: Z Wu & JM McGoogan, JAMA 323:1239, 2020.
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18

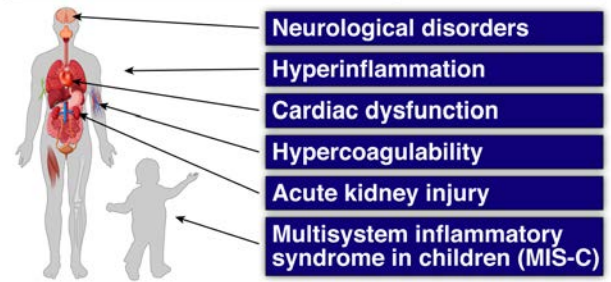
Manifestations of Severe COVID-19 Disease

- 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)

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19

Numerous Non-Pulmonary Complications of COVID-19 Have Been Reported

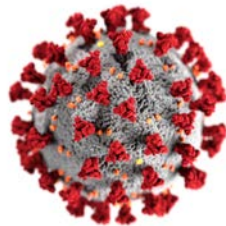


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20

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
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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

Source: CDC, 7/28/2020
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22

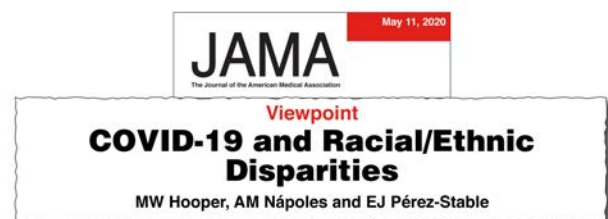
Underlying Medical Conditions That May Confer Increased Risk for Severe COVID-19 Illness

- | | |
|--|---------------------------------|
| ■ Asthma | ■ Inherited metabolic disorders |
| ■ Other chronic lung diseases | ■ Neurologic conditions |
| ■ Cerebrovascular disease | ■ Liver disease |
| ■ Diabetes, type 1 | ■ Pregnancy |
| ■ Hypertension | ■ Smoking |
| ■ Immunocompromised state from bone marrow transplant, immune deficiencies, HIV, use of corticosteroids or other immunosuppressive medications | ■ Thalassemia |

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Source: CDC, 7/28/2020

23

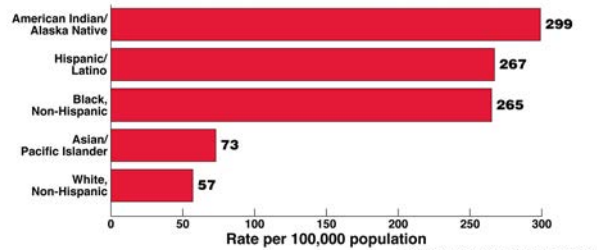


"The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations."

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24

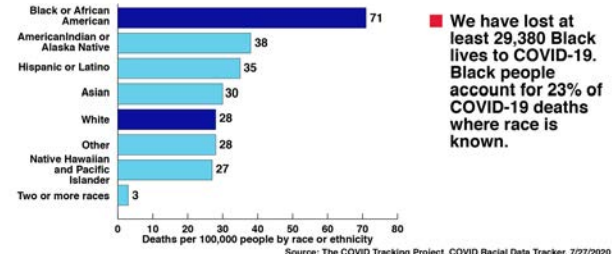
Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – July 25, 2020



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25

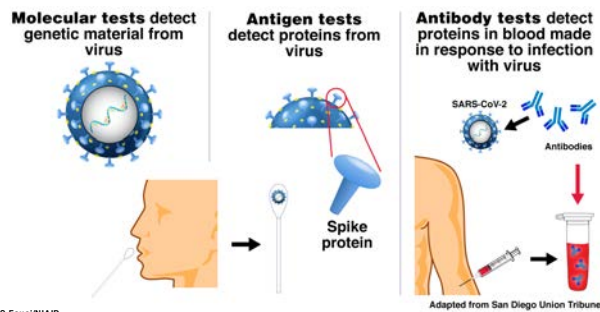
Nationwide, Black People are Dying at 2.5 Times the Rate of White People



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26

Tests for SARS-CoV-2



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27

NIH National Institutes of Health
Turning Discovery Into Health
Tuesday, April 21, 2020

News Release

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

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28

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



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29



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

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30



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

The RECOVERY Collaborative Group

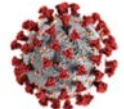
- RECOVERY trial in UK -- 6,425 patients randomized to receive dexamethasone 6 mg once per day (oral or IV) for up to ten days or usual care alone
- Dexamethasone reduced 28-day mortality by 36% in ventilated patients and by 18% in other patients receiving oxygen
- No benefit for patients not receiving respiratory support

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31

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

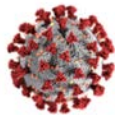


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32

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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33

THE LANCET

Published online June 1, 2020

Physical Distancing, Face Masks, and Eye Protection to Prevent Person-to-Person Transmission of SARS-CoV-2 and COVID-19: A Systematic Review and Meta-Analysis

DK Chu et al.

- 172 studies; n=25,697 patients.
- > 1 meter physical distancing associated with 82% reduction in infection; each additional meter doubled protection.
- Masks and respirators reduced risk of infection by 85%. Greater effectiveness in health-care setting than in the community.
- Eye protection reduced risk of infection by 78%.

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34



July 30, 2020

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

DJ McGrail, R Kalluri et al.

- 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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35



May 29, 2020

A Strategic Approach to COVID-19 Vaccine R&D








L Corey, JR Mascola, AS Fauci & FS Collins

- 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.

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36








Selected COVID-19 Vaccine Candidates

Platform	Developer	Phase 1/2	Phase 2/3
Nucleic acid	 moderna	Completed	Ongoing
	 BIONTECH	Completed	Ongoing
Viral vector	 UNIVERSITY OF OXFORD AstraZeneca	Completed	Ongoing
	 janssen	Ongoing	--
	 MERCK	TBD	--
Protein subunit	 NOVAVAX	Ongoing	--
	 gsk SANOFI	TBD	--

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37

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	 janssen	Ongoing	--
	 MERCK	TBD	--
Protein subunit	 NOVAVAX	Ongoing	--
	 gsk SANOFI	TBD	--

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38

NIH National Institute of Allergy and Infectious Diseases
July 27, 2020
News Release

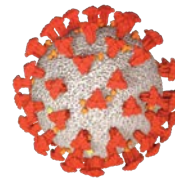
Phase 3 Clinical Trial of Investigational Vaccine for COVID-19 Begins

Multi-Site Trial to Test Candidate Developed by Moderna and NIH



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39



COVID-19
Prevention Network

coronaviruspreventionnetwork.org

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40