COVID-19 in 2021: Lessons Learned and Remaining Challenges

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- Epidemiology
- Virology
- Transmission
- Diagnostics
- Clinical Course
- Therapeutics
- Vaccines

COVID-19 in the United States

32.5 million cases
578,520 deaths

COVID-19 Globally

158.9 million cases
3,303,946 deaths

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

January 9, 2020

China Identifies New Strain of Coronavirus as Source of Pneumonia Outbreak
Daily New COVID-19 Cases Reported in the United States – Slopes of 3 Surges

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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

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

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.”
The Proportion of SARS-CoV-2 Infections That Are Asymptomatic

DP Oran and EJ Topol

- Available data suggest at least 1/3 of patients with SARS-CoV-2 infections never develop symptoms
- Longitudinal studies suggest ~3/4 of individuals with a positive PCR test who are asymptomatic at time of testing will remain asymptomatic

SARS-CoV-2 Transmission From People Without COVID-19 Symptoms

MA Johansson, JC Butler et al.

- 59% of all SARS-CoV-2 infections result from asymptomatic transmission
  - 35% from presymptomatic individuals
  - 24% from individuals who never develop symptoms

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

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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

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COVID-19 Clinical Presentation

- Fever: 83-99%
- Cough: 58-82
- 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

<table>
<thead>
<tr>
<th>Category</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild/Mod</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81%</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5%</td>
<td></td>
</tr>
</tbody>
</table>

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)

People at Increased Risk for Severe COVID-19 Illness

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

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Sequelea in Adults at 6 Months After COVID-19 Infection

- Approximately 30% of patients enrolled at U. of Washington reported persistent symptoms for as long as 9 months after illness
- Fatigue most commonly reported symptom
- Persistent symptoms were reported by one-third of outpatients with mild disease
Selected Therapeutics for COVID-19

- **Therapeutics for early/moderate disease**
  - Remdesivir – FDA approved
  - Monoclonal antibodies – EUA
    - Bamlanivimab, casirivimab-imsidavimab, andesivimab
    - Convalescent plasma – EUA
  - Other antivirals – clinical trials
  - Hyperimmune globulin – clinical trials

- **Therapeutics for moderate/advanced disease**
  - Dexamethasone – standard of care
  - Baricitinib+remdesivir – EUA
  - Immunomodulators (e.g. tocilizumab) – clinical trials
  - Anticoagulants – clinical trials

Identification of Vulnerable Targets in the SARS-CoV-2 Replication Cycle

- Design Drugs to Inhibit Vulnerable Targets

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**Selected COVID-19 Vaccines**

<table>
<thead>
<tr>
<th>Platform</th>
<th>Developer</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleic Acid (mRNA)</td>
<td>Moderna</td>
<td>EUA</td>
</tr>
<tr>
<td></td>
<td>BioNTech</td>
<td>EUA</td>
</tr>
<tr>
<td>Adenovirus Vector</td>
<td>Johnson &amp; Johnson</td>
<td>EUA</td>
</tr>
<tr>
<td></td>
<td>AstraZeneca</td>
<td>EUA TBO</td>
</tr>
<tr>
<td>Recombinant Protein and Adjuvant</td>
<td>Sanofi</td>
<td>EUA TBO</td>
</tr>
<tr>
<td></td>
<td>Novavax</td>
<td>EUA</td>
</tr>
</tbody>
</table>

**COVID-19 Vaccines are:**

- Efficacious in clinical trials
- Effective in real-world settings
- Safe

**Pfizer/BioNTech Vaccine**

**Moderna Vaccine**

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“Real World” Vaccine Effectiveness Studies

Estimated Effectiveness of 2 Doses of Pfizer/BioNTech COVID-19 Vaccine Against 6 Outcomes, Israel

Estimated Effectiveness of 2 Doses of Pfizer/BioNTech COVID-19 Vaccine Against SARS-CoV-2 Infection, by Age Group, Israel

Impact of Viral Variants on Vaccine Effectiveness
Wild Card: SARS-CoV-2 Variants

- **B.1.1.7** originally United Kingdom
  - Covering well by currently authorized mRNA vaccines; likely covered by J&J vaccine but more data needed
- **B.1.351** originally South Africa
  - Moderately to severely reduced vaccine efficacy for some vaccines - mRNA vaccine vs. placebo (moderate to severe disease); 2 doses efficacy vs. symptomatic disease; Pfizer/BioNTech 100% efficacy vs. asymptomatic disease; Moderna 94% efficacy vs. symptomatic disease (small numbers in critical data); Pfizer/BioNTech (late)
- **P.1** originally Brazil
  - Vaccine efficacy unknown (no clinical trials)
  - In vitro - moderate loss of neutralizing activity by vaccine-induced antibodies
- **B.1.429/B.1.427** originally California
  - Vaccines are likely still effective
  - In vitro - moderate loss of neutralizing activity by vaccine-induced antibodies
- **B.1.525** originally New York
  - Vaccine efficacy unknown
  - In vitro - variable loss of neutralizing activity by vaccine-induced antibodies
- **B.1.617** originally India
  - Vaccine efficacy unknown
  - In vitro - variable data

Effectiveness of the BNT162b2 COVID-19 Vaccine against the B.1.1.7 and B.1.351 Variants

- Mass vaccination campaign in Qatar; total 368,853
- Vaccine effectiveness against any documented infection
  - B.1.1.7 - 89.5% after 2 doses, 95.5% after 1 dose
  - B.1.351 - 75.0% after 2 doses, 66.9% after 1 dose
- Vaccine effectiveness against severe, critical, or fatal disease
  - B.1.1.7 - 100% after 2 doses, 84.1% after 1 dose
  - B.1.351 - 100% after 2 doses, 84.1% after 1 dose

Improved Neutralization of SARS-CoV-2 Variants After 2nd Pfizer Vaccine Dose

- **1 dose**
  - Week 2: 100% neutralization (RO$\geq 30$)
  - Week 4: 100% neutralization (RO$\geq 30$)
- **2 doses**
  - Week 2: 100% neutralization (RO$\geq 30$)
  - Week 6: 100% neutralization (RO$\geq 30$)

COVID-19 Vaccines are:

- Efficacious in clinical trials
- Effective in real-world settings
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Ensuring COVID-19 Vaccine Safety in the U.S.

- Clinical trials
- Expanded safety monitoring systems
  - CDC: V-safe
  - CDC: National Healthcare Safety Network (NHSN)
  - FDA: Other large insured/payer databases
- Other safety monitoring systems
  - CDC and FDA: Vaccine Adverse Event Reporting System (VAERS)
  - CDC: Vaccine Safety Datalink (VSD)
  - CDC: Clinical Immunization Safety Assessment (CISA) Project
  - FDA and the Center for Medicare and Medicaid Services: Medicare data
  - FDA: Biologics Effectiveness and Safety System (BEST)
  - FDA: Sentinel Initiative
  - DoD, VA systems

70% of adults vaccinated with at least 1 dose by July 4
The Race is On

SARS-CoV-2

Vaccines

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