Overview of COVID-19 Disease

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Dr. Brooks has no relevant financial affiliations to disclose
COVID-19
Virology
Basic Structure of *Coronavirinae*

- Single-stranded RNA viruses
- Genomes range from 25 to 32 kilobases
- The coronaviral genome encodes **four major structural proteins** (all are required to produce a structurally complete viral particle)
  - Spike (S) protein: *binding*
  - Nucleocapsid (N) protein: *RNA synthesis*
  - Membrane (M) protein: *organization/assembly*
  - Envelope (E) protein: *organization/assembly*
Electron Micrograph of Coronavirus Virions
**Coronaviridae/-virinae Belong to Order Nidovirales**

<table>
<thead>
<tr>
<th>Order</th>
<th>Nidovirales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family</td>
<td>Coronaviridae</td>
</tr>
<tr>
<td>Sub-family</td>
<td>Coronavirinae</td>
</tr>
<tr>
<td>Genera</td>
<td>Alpha-CoV</td>
</tr>
</tbody>
</table>

**Infect a wide variety of mammals and birds**
- Alpha and beta: “mammals”
  - flying bats to beluga whales
- Gamma and delta: “birds”
  - sparrows to ostriches

**Cause a variety of lethal diseases**, with well-studied impact on the agricultural sector
- Illness is usually **respiratory or enteric**
Seven Human Coronaviruses (HCoVs)

- **Common HCoVs (lower pathogenicity):**
  - HCoV-229E (alpha)
  - HCoV-NL63 (alpha)
  - HCoV-OC43 (beta)
  - HCoV-HKU1 (beta)

- **Other HCoVs (higher pathogenicity):**
  - SARS-CoV-1 (beta)
  - MERS-CoV (beta)
  - **SARS-CoV-2** (beta)  
  The illness COVID-19 is caused by SARS-CoV-2, which is more like SARS-CoV-1 than MERS-CoV

Song 2019, Viruses 11, 59; doi:10.3390/v11010059
COVID-19
Transmission
Linkage of Early COVID-19 Cases* to Huanan Seafood Wholesale Market – Wuhan, China

Adapted from Li 2020, N Engl J Med; DOI: 10.1056/NEJMoa2001316.

* Total N=324 persons with complete exposure histories among 425 total cases

https://www.healthpolicy-watch.org/
Early Distribution of Cases: China as of 20-Jan-2020
Distribution of COVID-19 cases in accordance with the applied case definitions in the affected countries, as of 05 March 2020

- **February 25**: Cases outside China exceed cases reports in China
- **March 4**: Deaths outside China exceed death reports in China

Courtesy of European CDC
Number of confirmed COVID-19 cases, by date of report and WHO region, 30 December through 23 June

~8,800,000
(last 24 hours 188,000)

~115,000

Valid as of June 20, 2020

https://covid19.who.int/
# Transmission Dynamics of Pathogenic Human Coronavirinae (CoV)

<table>
<thead>
<tr>
<th></th>
<th>SARS-CoV-1</th>
<th>MERS-CoV</th>
<th>SARS-CoV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation period, median (range)</td>
<td>4-6 days (up to 16)</td>
<td>4-6 days (range 2-14)</td>
<td>5 days (range 2-14)</td>
</tr>
<tr>
<td>Serial interval (days)</td>
<td>&gt; Incubation (8)</td>
<td>&gt; Incubation (12-14)</td>
<td>&lt; Incubation (4)</td>
</tr>
<tr>
<td>Infectious before ill</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**SARS-CoV-2**

- Peak infectiousness days before symptom onset (*pre-symptomatic*) and shortly thereafter
- A substantial fraction of infections, estimated 30-35%, are *asymptomatic*

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Park 2018, *BMC Public Health*; doi.org/10.1186/s12889-018-5484-8
## SARS-CoV-2 in Human Samples and Transmission

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mode of transmission</th>
<th>Detected by PCR</th>
<th>Isolated by culture</th>
<th>Observed mode of transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngeal swab</td>
<td>RESPIRATORY</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Oropharyngeal swab</td>
<td>RESPIRATORY</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sputum</td>
<td>RESPIRATORY</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Stool</td>
<td>FECAL</td>
<td>Yes</td>
<td>Yes but likely rare</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Urine</td>
<td>URINARY</td>
<td>No</td>
<td>Not yet reported</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Blood/serum</td>
<td>TRANSFUSION</td>
<td>No</td>
<td>No</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>PERINATAL</td>
<td>No</td>
<td>Not yet reported</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Umbilical cord blood</td>
<td>PERINATAL</td>
<td>No</td>
<td>Not yet reported</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Breast milk</td>
<td>SEXUAL</td>
<td>No</td>
<td>No</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Cervicovaginal fluid</td>
<td>SEXUAL</td>
<td>Yes, but likely rare</td>
<td>Not yet reported</td>
<td>Not yet reported</td>
</tr>
<tr>
<td>Semen</td>
<td></td>
<td>Yes, but likely rare</td>
<td>Not yet reported</td>
<td>Not yet reported</td>
</tr>
</tbody>
</table>

How Far Can SARS-CoV-2 Travel?

Respiratory droplets
About 6 feet (2 meters)

Airborne/aerosolized
Many meters
COVID-19
Response to Infection

Valid as of June 20, 2020
Viral Burden Declines Steadily After Illness Onset

Wölfel 2020, Nature; doi.org/10.1038/s41586-020-2196-x.
• Within days after symptom onset, patients beginning to develop serologic response to infection that includes IgM, IgG, and IgA.

• IgG response includes neutralizing antibodies.

• After 8-10 days, replication-competent virus can no longer be recovered from respiratory tract specimens, in otherwise healthy persons with mild to moderate illness.

• In severely ill and immunocompromised persons, shedding of culturable virus may persist up to 20 days.
Ability to Culture Virus from Specimens Declines with Decreasing Viral Burden

CDC, unpublished data.
PCR Can Remain Positive for Weeks After Recovery

Signs/Symptoms of COVID-19

- Fever
- Cough
- Myalgia/arthralgia
- Headache
- Diarrhea

Wuhan City (N = 138)
Hubei Province (N = 137)
China Country (N = 1,099)

Valid as of June 20, 2020
Signs/Symptoms of COVID-19

- No particular set of signs or symptoms can reliably discriminate COVID-19 from other respiratory viral illnesses such as influenza
  - Anosmia/dysgeusia
- Most people will recover spontaneously with supportive care
- Typical complications include pneumonia, respiratory failure, multiorgan system failure, and death

Illness Severity in Adults and Children with COVID-19, China

Severity of Illness, Adult COVID-19 (N = 44,672 confirmed cases)

- Mild: 80.9%
- Severe: 13.8%
- Critical*: 4.7%
- Missing: 0.6%

* 1,023 (49%) deaths among 2,087 critically ill adults

Severity of Illness, Pediatric COVID-19 (N = 2,141 confirmed cases)

- Moderate: 41.0%
- Severe: 2.5%
- Critical*: 0.4%
- Asymptomatic: 12.9%
- Missing: 0.1%

* 1 death among critically ill children

COVID-19 in High-Risk Groups

- Comorbidity and advanced age increase risk for severe illness and death
  - Cardiovascular disease, diabetes, chronic respiratory disease

- Immunocompromised (medical, acquired) – emerging data reassuring
  - For persons with HIV, risk likely greatest at low CD4 cell counts or not virally suppressed
  - No definitive evidence that cancer therapy worsens outcomes (incl. immunosuppressives)

Unique Complications of COVID-19

- **Diffuse endotheliitis**
  - Viral tropism for endothelial cells with inflammatory cell injury and death

- **Hypercoagulability**
  - Both local and embolic
  - ARDS complicated by thromboemboli (especially pulmonary embolism)

- **Peri- and post-infectious hyperimmune reaction**
  - Myocarditis (STEMI without coronary artery blockage)
  - Multiorgan inflammatory syndrome in children (MIS-C)

SARS-CoV-2 and Influenza Coinfection, Coinfection with Influenza B More Deadly

- Patients from a single hospital outbreak in Wuhan during Jan-Feb 2020
- Diagnoses made by assaying SARS-CoV-2 RNA and influenza IgM
- No significant differences in age (median 50’s-60’s), sex (M:F, 1:1), illness severity