COVID-19: The Virus, Transmission Dynamics & Clinical Aspects

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Objectives

At the end of this session, you will be:

1. Dazzled by the rapidly emerging science of COVID-19
2. Much less afraid than you are now
3. Able to share a vulgar display of recently acquired knowledge with your friends
The WHO declared a *Public Health Emergency of International Concern* around 2019-nCoV because of the spread of the virus outside of China, describing it as an “unprecedented outbreak”.
– January 30, 2020
Cases of coronavirus outside China

- 1 to 10
- 11 to 100
- 101 to 500
- 501 to 1,000
- More than 1,000
- No confirmed cases

Source: WHO, health ministries. Updated: 5 Mar 06:00 GMT
### COVID-19 as of March 5, 2020

<table>
<thead>
<tr>
<th>4-Mar-2052,045</th>
<th>Cases</th>
<th>Deaths</th>
<th>Severe</th>
<th>Recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>China</strong></td>
<td>80,409</td>
<td>3,012</td>
<td>5,952</td>
<td>52,045</td>
</tr>
<tr>
<td><strong>Outside China</strong></td>
<td>15,865</td>
<td>297</td>
<td>422</td>
<td>1,263</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>96,274</td>
<td>3,309</td>
<td>7,374</td>
<td>53,308</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Rates</th>
<th>Case Fatality</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.4%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Multiple sources
The Problem with COVID-19

**VELOCITY OF THE VIRUS**

For the first 1,000 people to be infected, MERS took **903 days or 2.5 years**

SARS took **130 days**

and the new coronavirus took **48 days**
Most cases are never counted

Cases detected in mainland China early in the outbreak

Deaths

Severe

Cases with symptoms (e.g. fever)

Mild cases (hardest to count)

Source: Imperial College London

Is this COVID-19?
The Virus
SARS-CoV-2 (COVID-19)

Pathogenesis of Infection in Humans

• SARS-CoV-2 enters human cells using the same doorway that SARS-CoV $\rightarrow$ ACE-2 (Angiotensin Converting Enzyme-2)

• ACE-2 is the receptor to which the Receptor Binding Domain (RBD) on the spike protein first attaches, enabling the virus to fuse with the host cell

• Target site is both upper respiratory tract and lower respiratory tract
  • Uncertain whether other tissues e.g. GI tract can act as portals

• The range for incubation (time of infection until time of first symptoms) is very broad when including rare cases (1-24 days)
Coronavirus Replication

SARS-CoV-2

ACE-2 Receptor

RBD on Spike Protein

Binding and cell entry

Host Cell

Virus

Cell receptors

RNA released

RNA replicated and packaged

Assembly

Nucleus

Replicated virus

Small changes

Release

Respiratory Epithelial Cell
The Origins of COVID-19 – Genomic Analysis

• 24 studied samples, including from Thailand and Shenzhen as well as Wuhan, show very limited genetic variation
  • This is indicative of a relatively recent common ancestor for all these viruses
  • The genome sequences suggest that this was a one-time jump as the genomes are very uniform

• Applying ballpark rates of coronavirus evolution, it is estimated that the Adam/Eve virus from which all others are descended first appeared between Oct 30 - Nov 29, 2019

• It is a mammalian coronavirus
  • 96% identical at the whole genome level to a bat coronavirus, not snakes
  • Pangolin connection?

Animal Coronaviruses and SARS-CoV-2 (COVID-19)

Origins and Evolution of SARS-CoV-2

The evolutionary relationships of the virus samples suggest a shared common ancestor sometime in November 2019.

SARS-CoV-2 Haplotype: L & S

- **S haplotype** is the ancestral form, which is associated with less aggressive disease
- **L haplotype** is a more evolved recent form, which is associated with more aggressive disease

Source: Tang X et al On the origin and continuing evolution of SARS-CoV-2 Microbiology 2020 in press
Impact of L vs. S Haplotypes on Case fatality rate

- Interventions placed more selective pressure on the L type, which may be more aggressive and spread more quickly.
- As a result, the S type, evolutionarily older and less aggressive, increased in relative frequency due to relatively weaker selective pressure.

Figure 6. The two types of SARS-CoV-2 showed differences in temporal and spatial distributions.

Source: Tang X et al On the origin and continuing evolution of SARS-CoV-2 Microbiology 2020 in press
SARS-CoV-2 Transmission Dynamics
Transmission Dynamics of COVID-19

• Primarily large droplet spread similar to influenza \(^2\)
  • Minimally symptomatic viral shedding – likely some transmission
  • Possible fomite transmission – limited data but likely
  • Possible fecal-oral transmission – limited data

• The mean incubation period = 5.2 days (95% CI, 4.1 to 7.0) \(^1\)
  • Maximal incubation 14-21 days

• The basic reproductive number (R0) = 2-3 (95% CI, 1.4 to 3.9)

Sources:
1. Qun Li et al Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia  NEJM DOI: 10.1056/NEJMoa2001316 - Jan 29, 2020
Comparative Transmission Rates of Various Viruses

(estimates as of mid-February)
The R0 is fluctuating in various countries
SARS-CoV-2 (COVID-19) Nasal > Throat Viral Shedding

- Analyzed the viral load in nasal and throat swabs obtained from the 17 symptomatic patients in relation to day of onset of any symptoms
- Higher viral loads were detected soon after symptom onset, with higher viral loads detected in the nose than in the throat
- Shedding pattern of patients infected with SARS-CoV-2 resembles that of patients with influenza

Source: Zou et al NEJM 2020 DOI: 10.1056/NEJMc2001737
COVID-19: The Complexity of Transmission
COVID-19: Estimated Attack Rate

• Symptomatic secondary attack rate = 0.45% (95% CI = 0.12%–1.6%) among all close contacts

• Symptomatic secondary attack rate = 10.5% (95% CI = 2.9%–31.4%) among household members

Clinical Aspects of COVID-19
Symptoms of COVID-19

Virus seems to start with a **fever**, followed by a **dry cough** and then, after a week, leads to **shortness of breath** and some patients needing hospital treatment.

- Headache
- Cough
- Muscle pain
- Fever & tiredness

Zhang Y et al Chinese J of Epidemiology http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51
# Signs & Symptoms in 99 patients with COVID-19

<table>
<thead>
<tr>
<th>Signs and symptoms at admission</th>
<th>Patients (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>82 (83%)</td>
</tr>
<tr>
<td>Cough</td>
<td>81 (82%)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>31 (31%)</td>
</tr>
<tr>
<td>Muscle ache</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>Confusion</td>
<td>9 (9%)</td>
</tr>
<tr>
<td>Headache</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Rhinorrhoea</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>More than one sign or symptom</td>
<td>89 (90%)</td>
</tr>
<tr>
<td>Fever, cough, and shortness of breath</td>
<td>15 (15%)</td>
</tr>
</tbody>
</table>

Chen et al Lancet 2020 https://doi.org/10.1016/S0140-6736(20)30211-7
Key Time-to-Event Distributions.

Source: Qun Li et al Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia NEJM
DOI: 10.1056/NEJMoa2001316 - Jan 29, 2020
COVID-19: Timeline of Illness

Huang C et al Lancet 2020  DOI: (10.1016/S0140-6736(20)30183-5
Clinical Defined Presentations of COVID-19

1. Uncomplicated illness  
2. Mild pneumonia  
3. Severe pneumonia  
4. ARDS
Chest Radiographs of COVID-19 Severe Pneumonia

COVID-19 Illness in China

- Mild: 80.9%
- Severe: 13.8%
- Critical: 4.7%
- Died: 2.3%

n = 72,314

COVID-19 Illness Trajectory

Figure 5. Pattern of disease progression for COVID-19 in China
COVID-19 fatality rate by age
Among diagnosed cases in Hubei, China, as of Feb. 11

Zhang Y et al Chinese J of Epidemiology http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51
Death rate varies by age, health and sex

Proportion of deaths among confirmed cases

Age

- 80+
- 70-79
- 60-69
- 50-59
- 40-49
- 30-39
- 20-29
- 10-19
- 0-9

Health condition

- Cardiovascular
- Diabetes
- Respiratory disease
- Hypertension
- None

Sex

- Male
- Female

Source: Chinese Centre for Disease Control & Prevention, 18 Feb 2020
Figure 4 Case fatality ratio (reported deaths among total cases) for COVID-19 in China over time and by location, as of 20 February 2020

Why?
- Faster case recognition
- More testing
- Better PPE
- Haplotype substitution
COVID-19 Case Fatality Rate in Perspective

**FATALITY RATE**

For every 50 people that were infected,
MERS killed **17 people**

SARS killed **five people**

and the new coronavirus killed **one**
My best guess
COVID-19 Patient Management

1. Uncomplicated illness
   • Manage as outpatient

2. Mild pneumonia
   • Consider admission if age >65 years

3. Severe pneumonia
   • Hospital admission for 5-6 days
   • O₂ and possible escalation of care

4. ARDS
   • ICU care for 2+ weeks
   • Prolonged mechanical ventilation
   • Possible use of ECMO

Links to Care Guidelines

UKPH Primary Care Guidance

WHO Clinical Care Guideline
COVID-19: Antivirals & Vaccine Strategies

• Antivirals
  • Remdesivir
  • Kaletra® (lopinavir/ritonavir) plus chloroquine
  • Oseltamivir

• Vaccine development
  • 12 months minimum to viable vaccine
COVID-19: Infection Prevention & Control
This is NOT a correct response to COVID-19
COVID-19: IPAC Definitions

**Person Under Investigation**

**Suspect** = Test ordered & results pending
- Symptoms and high-risk travel

**Presumptive** = PHL test positive
- Symptoms, travel & lab test positive

**Confirmed** = NML test positive

**Quarantined Person**

No signs and symptoms of ARI but High Risk Travel Exposure

14-day observation
Infection Prevention & Control in Health Care Settings

This

NOT this
Recommended measures for hospital staff dealing with coronavirus

- Isolate patients and limit their movement
- Wear protective clothing such as medical mask, eye protection, gloves and gown
- Disinfect shared equipment between patient use
- Wash hands after patient contact
Face masks compared

**N95 respirator**
Reduces exposure to small particles
Filters out at least 95% of airborne particles
Tight fitting, allows minimal leakage

**Surgical mask**
Fluid resistant, protects wearer against large droplets
Does not protect against smaller airborne particles
Loose fitting - allows leakage around the edges

Source: 3M, Getty
### Ontario Planning scenarios

<table>
<thead>
<tr>
<th>Scenario 1: Travel-related Cases</th>
<th>Scenario 2: Ontario Outbreak</th>
<th>Scenario 3: Global Pandemic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No or limited community</td>
<td>• Ongoing community</td>
<td>• Ongoing community</td>
</tr>
<tr>
<td>transmission</td>
<td>transmission in Ontario</td>
<td>transmission in every</td>
</tr>
<tr>
<td>• Cases have travel history</td>
<td>but not in every region of</td>
<td>region of the world,</td>
</tr>
<tr>
<td>(or close contact to a confirmed</td>
<td>the world</td>
<td>including Ontario</td>
</tr>
<tr>
<td>case or asymptomatic case)</td>
<td>• Community spread in</td>
<td>• Community based spread</td>
</tr>
<tr>
<td>• Low risk to the community</td>
<td>Ontario leading to an</td>
<td>in multiple locations in</td>
</tr>
<tr>
<td>• High risk of ‘imported’ cases</td>
<td>outbreak (n&lt;500, similar to</td>
<td>Ontario</td>
</tr>
<tr>
<td>(n&lt;50 over 6 months)</td>
<td>the 2003 SARS outbreak)</td>
<td>• PPE manufacturers can no</td>
</tr>
<tr>
<td>• PPE manufacturers are</td>
<td>• Ontario would be a higher</td>
<td>longer prioritize regions</td>
</tr>
<tr>
<td>prioritizing global regions</td>
<td>priority in the global</td>
<td>as all areas are</td>
</tr>
<tr>
<td>with active outbreaks</td>
<td>supply chain as region</td>
<td>experiencing outbreaks</td>
</tr>
<tr>
<td></td>
<td>with an active outbreak</td>
<td></td>
</tr>
</tbody>
</table>

We are here!
COVID-19 Summary – March 5, 2020

• Cases have been overwhelming seen in China (86%)
  • Cases rising outside of China

• This is an easily transmitted virus, but NOT a highly transmissible one

• The disease is a respiratory one with severe illness requiring hospitalization in about 10-15%, most of whom are >70 years old
  • If large number of minimally symptomatic cases are not being counted the CFR is likely 0.2-0.3%

• Do NOT wear a mask in public unless you are ill

• If a case is suspected, there are procedures to identify, follow and manage patients in the community (KFLA Public Health) and the hospital (KHSC)
“Hand over your Purell.”