Temas de discusión

• Human coronaviruses in general, SARS, MERS and the novel coronavirus, SARS-CoV-2
• The emergence of SARS-CoV-2 and its associated disease (COVID-19) in Wuhan, China
• Symptoms and treatment
• Individual-level prevention
• Population-level prevention
• Impact and the future
Coronaviruses

• Before SARS (2002), coronaviruses were considered relatively inconsequential pathogens that caused common colds
  • Four human coronaviruses are endemic globally and cause 10-30% of upper respiratory tract infections in adults (alpha coronaviruses HCoV 229E, NL 63, OC 43, HKU 1)

• Widely distributed in mammals and birds

• Since 2002 we’ve recognized two highly pathogenic strains that causes severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)
SARS and MERS

- As opposed to the human coronaviruses that are associated with upper respiratory tract infections, SARS and MERS are caused by beta coronaviruses.
- Primarily cause lower respiratory tract infection (pneumonia).
- Relatively high case fatality rates.

<table>
<thead>
<tr>
<th></th>
<th>SARS</th>
<th>MERS</th>
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</thead>
<tbody>
<tr>
<td>Cases</td>
<td>8098</td>
<td>2494</td>
</tr>
<tr>
<td>Deaths</td>
<td>774</td>
<td>858</td>
</tr>
<tr>
<td>Case fatality rate</td>
<td>9.5%</td>
<td>34.4%</td>
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<tr>
<td>Controlled</td>
<td>Yes after reached pandemic</td>
<td>No, continued transmission</td>
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<tr>
<td>Other features</td>
<td>58% from nosocomial transmission</td>
<td>70% of cases from nosocomial transmission</td>
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Emergence of the 2019 novel coronavirus (SARS-CoV-2)

- First case (COVID-19) hospitalized 17 December 2019
- Cluster reported on 30 December
- Huanan Wholesale Seafood Market closed 1 January
- COVID-19 isolated 7 January
- COVID-19 sequenced 10 January
- Rapid diagnostic tests developed and distributed
- *Cordon sanitaire* implemented in Wuhan and surrounding cities on 23 January – 59 million people quarantined
- WHO declared Public Health Emergency of International Concern 30 January
- Outbreak grew from a handful of cases exposed at Huanan wholesale seafood market to more than 250,000 cases and 10,000 deaths in less than 3 months with ongoing person-to-person transmission primarily via respiratory droplet
Respiratory spread

• Data suggest similar transmission as seasonal influenza
  • Droplet - primary, large virus-laden nuclei, <6 feet (OSHA) or <1 m (WHO), don’t stay in air
  • Hands
  • Fomites (surfaces)
  • Possible: gastrointestinal
  • While theoretically possible, aerosol transmission unlikely

• Infection control needs to focus on *droplet spread*, which is far and away the most common route of transmission, followed by fomite and possibly GI
Epizooology of COVID-19

- Genetic sequence close to bat strains of coronavirus
- Suggestion of a secondary host, which acquired COVID-19 from bats and transmitted it to humans at Huanan Wholesale Seafood Market
- Possible candidate is the *pangolin*, a mammal whose scales used in traditional medicine
  - Most illegally trafficked animal in the world
Egypt is first new country in over a week. Iran is the only new country to report cases in the last 5 days. Secondary outbreaks in South Korea, Italy and Iran.
Most western countries are on the same coronavirus trajectory. Hong Kong and Singapore have so far limited the spread; S Korea is slowing its progress.

Cumulative number of cases, by number of days since 100th case

China had 58,761 cases at 25 days

S Korea: mass testing and quarantine have slowed the spread

Japan: there is debate over whether the spread has slowed or there are simply not enough tests being done

Singapore: strict quarantine rules and contact tracing

Hong Kong: school closures and quarantine, strong community response

FT graphic: John Burn-Murdoch / @jburnmurdoch
Source: FT analysis of Johns Hopkins University, CSSE. Data updated March 14, 19:00 GMT © FT
On 18 March China reported no new domestic cases. All 34 new cases were imported.
FIGURE 2. COVID-19 hospitalizations, * intensive care unit (ICU) admissions, † and deaths, § by age group — United States, February 12–March 16, 2020

* Hospitalization status missing or unknown for 1,514 cases.
† ICU status missing or unknown for 2,253 cases.
§ Illness outcome or death missing or unknown for 2,001 cases.

Cases in California, 19 March 2020

- 870 cases and 16 deaths
  - At least 60 local transmissions
- Testing still lagging
- California bans gatherings of >50 people
- Disneyland announces closure

- >11 900 self monitoring who returned to the U.S. through LAX or SFO
- 49 local health jurisdictions involved in self monitoring
- 8 316 tests done in 21 public health labs
- 21 public health, several university labs and 2 commercial labs with test kits - moving to 5 500 tests per day
Figure 2. Description of the known transmission chain of event originating in Singapore (Event Number 1, Table 1), as of 10 am 13 Feb 2020

- **Singapore Conference** (7 confirmed cases)
  - **Singapore** (3 cases)
  - **Republic of Korea** (2 cases)
  - **The United Kingdom** (1 case)
  - **Malaysia** (1 case)

- **French chalet** (11 confirmed cases)
  - **The United Kingdom** (5 cases)

- **France** (5 cases)

- **Spain** (1 case)

- **Malaysia** (2 cases)
  - Last reported to WHO 09/02/20

(As of 10 am 13 Feb)
Current understanding of clinical COVID-19

- Most likely single introduction to humans then person-to-person spread
- $R_0$ 2.68 (95% confidence interval 2.47-2.86)
- Doubling time 6.4 days
- Incubation period 5.2 days (may be as long as 14)
- Median age 49-56 years, cases very rare in infants and children
- Virus shedding can occur 24-48 hours before onset of symptoms and continues for 7-12 days in mild/moderate, >14 days in severe disease

- Nonspecific symptoms: fever and dry cough in majority, one-third dyspnea
- 5% of patients with develop ARDS and require intensive care, 20% may need hospitalization for clinical reasons
  - Particularly true for those with comorbid conditions, like diabetes or hypertension
COVID-19 testing per million inhabitants by country*

*As of 9 March 2020

Source: Tomas Puyo analysis from data aggregated by Worldometers: https://www.worldometers.info/coronavirus/covid-19-testing/
Per country sources available at Worldometers or at:
https://docs.google.com/spreadsheets/d/1YyCmjb2Z2QwMnFwAb7IVdVQoEAiL9CoQARsi03dSw/edit#gid=509476859
New therapeutics and vaccine

• Remdesivir (Gilead)
  • Broad spectrum antiviral compound with in vitro activity against SARS-CoV-2 and MERS
  • Nucleotide analogue
  • Phase 2 trials have begun at University of Nebraska National Quarantine Unit, where sickest COVID-19 patients evacuated from Asia are hospitalized

• Lopinivir/ritonavir combination therapy under study in China
  • Targets SARS-CoV-2’s protease enzyme
  • RCT found no effect (18 March)

• Moderna Therapeutics shipped first vials of a COVID-19 vaccine to NIAID for initial testing on February 25 (one of three candidate vaccines)
  • 42 days after initial sequencing were made available

• NIAID will likely begin early clinical safety trials in April
  • It will take 1.5 years to fully test

Note: there are 94 trials registered at clinicaltrials.gov and 423 at ICTRP
Two strategic goals

• Limit new cases by decreasing $R_e$, the effective reproductive number

• Flatten and prolong the outbreak to (1) assure adequacy of health care resources and (2) buy time for antivirals and eventually vaccine
Effects of pandemic mitigation on health care needs

- Delay epidemic peak
- Reduce height of peak
- Spread cases over a longer time period
- Unmet need
Modeling outcomes

Projected daily mortality due to COVID-19, US and UK

Critical care bed capacity for COVID-19 by mitigation strategies, UK
Will it work?

• Two adjacent Italian provinces in Lombardy region
• One (Lodi) began shelter-in-place on 26 February
• Other (Bergamo) began shelter-in-place on 9 March
• Empirical evidence that shelter in place orders can blunt transmission and new disease
How will this end?

• Containment – didn’t happen
  • Keep large bulk of infection in China (currently 89%)
  • But large new clusters in Iran, Italy and South Korea with regional spread
  • New clusters of transmission will aggressive follow up, isolation and quarantine
  • Spring weather may give us a break
  • Key: rapid response to suspected cases
  • Can Italy and the EU contain their outbreaks?

• Pandemic spread – this is where we are now
  • Spread outside of China and sustained person-to-person transmission in other countries
    • Iran, Italy and South Korea
    • U.S. (New York, Washington, California)
  • Attack rate somewhere between <1% and 20% (40-70% in worst case scenarios with no controls)
  • Potentially very taxing on healthcare system (5% with critical disease)
  • Endemic cause of viral pneumonia?
  • Summer Olympics in Tokyo – what will happen?
DOUBLE FEATURE COMING SOON:

DEATH OF THE CORONAVIRUS

PLUS, END OF DONALD TRUMP