Using Infectious Dose to Understand Risk

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What About Dose?

- For SARS, highest risk of infection occurred during aerosol-generating medical procedures
- COVID-19 shows higher attack rates in indoor clusters
- Suggests that SARS and COVID-19 infections may be related to dose
  - Concentration & Time
Aerosol Transmission = Inhalation of Infectious Particles

- The probability of getting infected depends on inhaling an “infectious dose” = the number of virions needed to make infection likely
  - Function of where particles land in the lung
  - Likelihood of deposition
- Infectious dose does not necessarily imply illness (symptoms and disease)
- Don’t know infectious dose for COVID-19, but might estimate 1000 virions by analogy to influenza and other coronaviruses

https://www.medrxiv.org/content/10.1101/2020.05.21.20108894v2
Infectious Dose

- Viral load (RNA copies per mL) in sputum = viral load in particles emitted during breathing, talking, coughing, sneezing, etc.
- Viral emission rate is a function of:
  - Viral load in sputum
  - Volume of air exhaled per breath
  - Breathing rate
  - Number of particles emitted per breath
  - Volume of a particle (function of particle diameter)

**STEADY STATE CONCENTRATION**

Steady state concentration of infectious virus in the air (C, virions/m$^3$) is a function of:

- Generation rate of virions by infectious person (G, virions/min)
- Ventilation rate (Q, m$^3$/min)

$$C = \frac{G}{Q}$$

Person infected with SARS-CoV-2 generates 1000 virions/nL saliva.**

<table>
<thead>
<tr>
<th>Human Activity</th>
<th>Volume of Saliva</th>
<th>virions/min (G)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sneeze</td>
<td>1 μL (1000 nL)</td>
<td>$10^6$ (1 sneeze/min = 1,001,000/min)</td>
</tr>
<tr>
<td>Cough</td>
<td>100 nL</td>
<td>$10^5$ (1 cough/min = 101,000/min)</td>
</tr>
<tr>
<td>Talking</td>
<td>10 nL/min</td>
<td>$10^4$</td>
</tr>
<tr>
<td>Breathing</td>
<td>1 nL/min</td>
<td>$10^3$</td>
</tr>
</tbody>
</table>


STEADY STATE CONCENTRATION

Ventilation rate \((Q, \text{m}^3/\text{hr})\) is function of:
- Number of Air Changes per Hour \((\text{ACH}) (n)\)
- Volume of the room \((V, \text{m}^3)\)

\[
Q = nV
\]

**Example**
Room volume \((V) = 300 \text{ m}^3\) and \(\text{ACH} = 5\)
\(Q = 1500 \text{ m}^3/\text{hr}\) or \(26 \text{ m}^3/\text{min}\)

EXAMPLE — HOTEL ROOM

What’s the concentration in a 300 m³ hotel room with 5 ACH if an infectious guest stays overnight (12 hrs)?

Assume mostly breathing (90%), some talking (10%) & periodic coughing (1/hr).

<table>
<thead>
<tr>
<th>Activity</th>
<th>Calculation</th>
<th>G (virions/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing</td>
<td>0.9 x 10³ virions/min</td>
<td>900</td>
</tr>
<tr>
<td>Talking</td>
<td>0.1 x 10⁴ virions/min</td>
<td>1000</td>
</tr>
<tr>
<td>1 cough/hr</td>
<td>10⁵/hr x (hr/60 min)</td>
<td>1667</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>3567</td>
</tr>
</tbody>
</table>

\[ C = \frac{G}{Q} = 3567 \text{ virions/min} \div 26 \text{ m}^3/\text{min} = 137 \text{ virions/m}^3 \]
HOW LONG TO WAIT FOR ROOM TO CLEAR?

Time to wait for a room to clear is a function of the room volume, ventilation rate, and initial concentration:

\[ t_2 = -\frac{V}{Q} \ln \left( \frac{c_2}{c_1} \right) \]

Example: If we want the concentration to be no more than 0.1 virions/m\(^3\) (\(c_2\)), then the wait time is:

\[ -\frac{300 \text{ m}^3}{26 \text{ m}^3/\text{min}} \ln \left( \frac{0.1 \text{ virions/m}^3}{137 \text{ virions/m}^3} \right) = 84 \text{ min} \]
<table>
<thead>
<tr>
<th>ACH</th>
<th>99% minutes required</th>
<th>99.9% minutes required</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>138</td>
<td>207</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
<td>104</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>69</td>
</tr>
<tr>
<td>12</td>
<td>23</td>
<td>35</td>
</tr>
<tr>
<td>15</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>20</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>50</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>400</td>
<td>&lt;1</td>
<td>1</td>
</tr>
</tbody>
</table>
MIXING FACTOR

- The well-mixed box model assumes perfect mixing, which may not always be the case.
- Some guidelines suggest using a mixing factor \((m)\) to adjust the ventilation rate \((Q)\) where \(m\) could range from 0 (no mixing) to 1 (perfect mixing).

\[
C = \frac{G}{mQ}
\]

- Typically, values for \(m\) range from 0.1 to 0.5.
- Not entirely correct to use a mixing factor, because it violates the mass balance principle. Not used much in modeling.
WHAT'S THE EXPOSURE?

- What if one person in the room is infectious and the other is not?
- Steady state concentration = 137 virions/m³
- Dose (D) is a function of concentration (C), breathing rate (Q_{BR}) and time (t):
  \[ D = C Q_{BR} t \]

Someone sharing the room with this person, for 12 hours, breathing at a rate of 10 L/min (0.01 m³/min) will have a dose of 986 virions.
Estimate the probability of infection:

\[ P(\text{infection}) = 1 - \exp\left(-\frac{D}{D_{\text{infectious}}}\right) \]

\( D_{\text{infectious}} = \) infectious dose = 1000 virions (estimated; not known for SARS-CoV-2)

A dose of 986 virions has a 62% chance of leading to an infection.

INTERVENTIONS

- Source controls:
  - Limit the number of people staying in a room
  - Screen guests

- Pathway controls:
  - Increase HVAC ventilation rate (ACH) to decrease wait time [not always possible]
  - Add a portable air cleaner to the room to increase ventilation rate & decrease wait time [should have a high-efficiency filter]
  - Limit the amount of time a worker spends in a room
  - Limit the number of rooms cleaned