AIRBORNE INFECTIOUS DISEASE

* ≃ 25% of global deaths* = infectious disease
  ≃ 57 M deaths/year. (≃ 60 M/year)

* Deaths due to viral respiratory infections (WHO)
  ≃ 4.2 M/year
  ≃ 7% of global burden of disease.
  > 25% of death by infectious disease.

* Airborne infection = major route of infection

* Some examples:
  - Rhinovirus ⇒ most common viral infection in humans
    cause of "common cold".
    ≃ 99 types → differ by surface proteins.
    ≃ 30 - 300 nm. (Viruses are small!)
  - Influenza (H1N1, etc.) ⇒ RNA viruses (flu) Varies by season
    global = 250,000 - 500,000 deaths/yr.
    U.S. ≃ 3,000 - 50,000 deaths/yr.
  - Measles (highly contageous)
  - Severe acute respiratory syndrome (SARS)
    - severe pneumonia
  - Smallpox. (effectively eradicated), but 300-500 M deaths (20th century)
    ↗ Huge Disease irradication.
  - Canine distemper.
  - Tuberculosis (≠ virus) → bacterial infection. (horrible disease)

* Our goal:
  - Become familar w/ (conversant.) ⇒ 

  - Derive equations to predict probability of disease transmission
  - Use CO_2 to estimate re-breathed fraction.
  - Derive method to predict critical re-breathed fraction. (allows estimates of minimum acceptable ventilation rate).

DERIVATION OF WELLS-RILEY EQUATION

$P = \frac{D}{S}$ = probability that a susceptible individual becomes infected.

- D = # of disease cases
- S = # of susceptible individuals. (those not already w/ disease)

$$P = 1 - e^{-\bar{\mu}}$$ (poisson distribution)

$\bar{\mu}$ = average # of "quanta" breathed by a susceptible person (obviously makes probability of infection go up)

As $\bar{\mu}$ gets large $P \to 1$

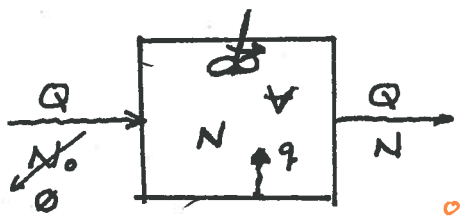
quantum = # of infections droplet nuclei necessary to initiate infection, based on assumption that infection requires at least one organism.

* strong function of type of infectious agent
* Highly infectious, e.g., measles, = high quantum generation rate.

$$\bar{\mu} = p_b t \bar{N}$$

p_b = breathing rate (what we called Q_B)
t = total time of exposure.
$\bar{N}$ = average quantum "concentration" (quanta/m^3)

Begin "quanta" balance (like mass balance)



Assumptions:

* Air space well mixed.
* Air exchange rate >> (Important)
  - loss of agent viability
  - loss by filtration
  - loss by settling/deposition.

(OR all rolled into estimate for q.)

variables:

* Q = ventilation rate (m^3/hr)
* $\forall$ = volume of occupied space (m^3)
* q = quantum generation rate by infected person (quanta/hr)
* N = quantum concentration (quanta/m^3)

q = "infectious source strength".

q = generation rate of infectious doses (NOT organisms or particles!!)

Mass balance on well-mixed Air space:

$$\forall \frac{dN}{d\theta} = Iq - N\mathcal{Q}.$$

accumulation = emission − loss (only air exchange)

θ = time = 0 when building 1st occupied.

I = # infected individuals

$$\frac{dN}{Iq - N\mathcal{Q}} = \frac{1}{\forall} d\theta \quad \therefore \quad \int_0^N \frac{dN}{Iq - N\mathcal{Q}} = \frac{1}{\forall}\int_0^\theta d\theta$$

Let $x = Iq - N\mathcal{Q}$.

$$\therefore \frac{dx}{dN} = -\mathcal{Q} \quad \therefore \quad dN = -\frac{1}{\mathcal{Q}} dx \quad \therefore$$

$$-\frac{1}{\mathcal{Q}}\int \frac{dx}{x} = \frac{\theta}{\forall} \quad \therefore \quad \int \frac{dx}{x} = -\frac{\mathcal{Q}}{\forall}\theta$$

$$\ln\left\{\frac{Iq - N\mathcal{Q}}{Iq - N(t=0)\mathcal{Q}}\right\} = -\lambda\theta \quad \therefore \quad \ln\left\{1 - \frac{N\mathcal{Q}}{Iq}\right\} = -\lambda\theta$$

($N(t=0) = 0$)

$$\left\{1 - \frac{N\mathcal{Q}}{Iq}\right\} = e^{-\lambda\theta} \quad \therefore \quad 1 - e^{-\lambda\theta} = \frac{N\mathcal{Q}}{Iq}.$$

$$\therefore N = \frac{Iq}{\mathcal{Q}}\left\{1 - e^{-\lambda\theta}\right\}$$

Now - calculate average quantum concentration from 0 to θ.

$$\bar{N} = \frac{1}{\theta}\int_0^\theta N\, d\theta = \frac{1}{\theta}\int_0^\theta \frac{Iq}{\mathcal{Q}}\left(1 - e^{-\lambda\theta}\right) d\theta$$

$$\bar{N} = \frac{Iq}{\theta\mathcal{Q}}\int_0^\theta \left(1 - e^{-\lambda\theta}\right) d\theta = \frac{Iq}{\theta\mathcal{Q}}\left\{\int_0^\theta d\theta - \int_0^\theta e^{-\lambda\theta} d\theta\right\}$$

$$\bar{N} = \frac{Iq}{\theta\mathcal{Q}}\left\{\theta - \frac{1}{\lambda}\left(1 - e^{-\lambda\theta}\right)\right\}$$

$$\bar{N} = \frac{Iq}{\mathcal{Q}}\left\{1 - \frac{1}{\lambda\theta}\left(1 - e^{-\lambda\theta}\right)\right\}.$$

(make sense?)

Steady-state? $\lambda\theta$ large.

$$\boxed{\bar{N} = \frac{Iq}{\mathcal{Q}}.}$$

As I or q up or $\mathcal{Q}$ ↓ the "infectivity" of air increases!

substituting $\bar{N} \rightarrow \bar{\mu}$ yields:

$$\bar{\mu} = p_b t \bar{N} = p_b t \frac{Iq}{Q}\left\{1 - \frac{1}{\lambda\theta}\left(1 - e^{-\lambda\theta}\right)\right\}$$

Recall: $P = \frac{D}{S} = 1 - e^{-\bar{\mu}}$, quanta/hr generation rate.

* $\therefore P = 1 - \exp\left\{\frac{-Iqp_b t}{Q}\left(1 - \frac{1}{\lambda\theta}\left[1 - \exp(-\lambda\theta)\right]\right)\right\}$

* Dynamic Wells-Riley Equation: (Classic model)

when $\lambda\theta$ becomes large

* $P = 1 - \exp\left\{\frac{-Iqp_b t}{Q}\right\}$ } steady-state Wells-Riley Equation.

Note effect of individual factors

* $P = \frac{D}{S}$ = probability of infection for susceptibles.
  - D = # of disease cases
  - S = # of susceptibles = n − I
  - n = # of people
  - I = # of infectors.

* Requirements: I, q, p_b, t, Q. } • steady-state • well-mixed. • no other losses but air exchange. (or lumped into q)

* q: from epidemiology data & back-calculation:

SOME VALUES of q. (quanta/hour) } Best-fit parameter to model w/ outbreaks in well-characterized environment

* Rhinovirus-16 ~ 1–10/hr.
* Pulmonary tuberculosis ~ 1–10/hr.
* Influenza ~ 100/hr. (order of). $\bar{X}$ = 67/hr (Liao et al.)
* Measles ~ 570/hr. (hugely infectious)
* SARS ~ 29/hr. (Liao et al.)

Flu: 1–100 ×
Cold

RUDNICK-MILTON EQUATION

} Alternative to Wells-Riley equation. Now commonly used.

* Get to P with CO_2 measurement.
* NO need for Q.!!!
* NO need for steady-state.

} significant advantage.

Rebreathed Fraction: (well-mixed air space)

* $(C - C_o)\forall$ = total volume of CO_2 generated by indoor sources. (assumes people)
  - C = indoor, C_o = outdoor
  - Vol. fraction CO_2
  - $\forall$ = total volume of indoor space. (m^3)

* $C_a \forall_e$ = volume of CO_2 from occupants.
  - C_a = vol. fraction of CO_2 added to exhaled breath by occupants. (volume fraction of CO_2 on breath)
  - $\forall_e$ = equivalent vol. of exhaled breath contained in indoor air. (m^3)

$C_a \forall_e = (C - C_o)\forall$ } assuming only indoor sources = humans.

f = fraction of indoor air that is exhaled breath = rebreathed fraction. — f up as C ↑

* $$f = \frac{\forall_e}{\forall} = \frac{C - C_o}{C_a}$$

} Easily measured parameters! NOTE: $f = \frac{\forall_e}{\forall} = \frac{\dot{\forall}_b}{\dot{Q}} = $ S-S PIF!!! $= \frac{\sum \dot{Q}_b}{\dot{Q}}$

Example: $C - C_o$ = 700 ppm = 700×10^{-6} (ASHRAE).

C_a = 38,000 ppm. = 0.038 ↑ vol. fraction.

$$f = \frac{700 \times 10^{-6}}{0.038} = \frac{7.0 \times 10^{-4}}{0.038} = 0.018 = 1.8\%$$

vegetarian!

ASHRAE 62.1-2013 generally says that this is "acceptable"

$\bar{f}$ = average fraction of indoor air that is exhaled breath, over total exposure period t.

$$\bar{f} = \frac{1}{t}\int_0^t f\,dt$$

} can integrate if measure indoor CO_2 during exposure period t.

$$f = \frac{C - C_o}{C_a}$$

Derivation of Rudnick-Milton Probabilistic Infection Equation:

* Let β = volume fraction of air in space that was exhaled by infectious persons (infectors)

$$\beta = f\frac{I}{n}$$

$\frac{I}{n} = \frac{V_e}{V}$

} I = # of infectors. n = # of people in the space.

* Let q/p_b = concentration of quanta in exhaled breath of infectors (quanta/m^3)

- q = quanta/sec. (quanta emission rate)
- p_b = m^3/sec

} Like $\frac{E}{Q} = C$

* N = quantum concentration in the ventilated space. $\left(\frac{\text{quanta}}{m^3}\right)$

$$N = \beta\left\{\frac{q}{p_b}\right\} = \frac{fIq}{np_b}$$

$\bar{N}$ = average quantum concentration over total exposure period t.

$$\bar{N} = \frac{\bar{f}Iq}{np_b}$$

* Let $\bar{\mu}$ = average # of quanta breathed by a susceptible person.

$$\bar{\mu} = p_b t \bar{N}$$

$= \frac{m^3}{s}$ s $\frac{\text{quanta}}{m^3}$ $= \text{quanta}$ } Taken as dimensionless

* $P = 1 - e^{-\bar{\mu}}$ } probability that a susceptible person becomes infected.

$\therefore P = 1 - \exp(-p_b t \bar{N})$ but $\bar{N} = \frac{\bar{f} I q}{n p_b}$

$= 1 - \exp\left(-p_b t \frac{\bar{f} I q}{n p_b}\right)$ $= \frac{D}{S} = \frac{\#\text{ of disease cases}}{\#\text{ of "susceptibles"}}$.

* $$P = 1 - \exp\left(-\frac{\bar{f} I q t}{n}\right)$$ Rudnick - Milton equation.

• discuss

IMPORTANT

* ~~Assume well-mixed space (not near-field)~~ * Important
* Valid for both steady-state & non-steady state !!!
* Valid even if Q varies with time (Q = ventilation rate)
* q often determined ~~from~~ back-calculation of values recorded from case studies.
  - know D, S, (& P), I, $\bar{f}$, t, n ⟶ get q.

Can estimate if do not have measured CO_2. How?

* Aircraft
* schools
* prisons
* etc.

Reproductive Number in Shared Indoor Space.

R_0 = Basic reproductive number = # of secondary infections that arise when a single infectious case is introduced into a population where everyone is susceptible.

$R_0 > 1 \Rightarrow$ agent spreads in population.

Larger R_0 = more likely an epidemic occurs.

* Let R_{AO} = reproductive number for an infectious disease in a building environment.

* Rudnick-Milton Equation: $P = 1 - \exp\left(\frac{-\bar{f} I q t}{n}\right) = \frac{D}{S}$

  - Let $I = 1$ (single infectious case)
  - S = # susceptibles $= n-1$

$\therefore \quad \frac{D}{S} = \frac{D}{n-1} = 1 - \exp\left(\frac{-\bar{f} q t}{n}\right)$

$\therefore \quad \boxed{D = R_{AO} = (n-1)\left\{1 - \exp\left(\frac{-\bar{f} q t}{n}\right)\right\}}$

Want < 1 !!

CRITICAL RE-BREATHED FRACTION. ($\bar{f}_c$)

* would like $\bar{f}_c$ so that $R_{AO} < 1$.
* set $R_{AO} = 1$ and solve for $\bar{f}$ $(= \bar{f}_c)$

$$R_{AO} = 1 = (n-1) - (n-1)\exp\left(\frac{-\bar{f}_c q t}{n}\right)$$

$$\therefore \quad 1-(n-1) = -(n-1)\exp\left(\frac{-\bar{f}_c q t}{n}\right)$$

$$(2-n) = \quad " \qquad\qquad "$$

$$(n-2) = (n-1)\exp\left(\frac{-\bar{f}_c q t}{n}\right)$$

$$\frac{(n-2)}{(n-1)} = \exp\left(\frac{-\bar{f}_c q t}{n}\right)$$

Taking ln both sides:

$$\ln\left\{\frac{n-2}{n-1}\right\} = \frac{-\bar{f}_c q t}{n} \quad \therefore \quad -\ln\left\{\frac{n-2}{n-1}\right\} = \frac{\bar{f}_c q t}{n}$$

$$\therefore \quad -n \ln\left\{\frac{n-2}{n-1}\right\} = \bar{f}_c q t$$

$$\therefore \quad \bar{f}_c q t = \ln\left\{\frac{n-1}{n-2}\right\}^n$$

$$\therefore \quad \boxed{\bar{f}_c = \frac{1}{qt} \ln\left\{\frac{n-1}{n-2}\right\}^n}$$

CRITICAL RE-BREATHED FRACTION.

For $n > 30$

$$\boxed{\bar{f}_c \simeq \frac{1}{qt}}$$

Example (Engineering Analysis) Rhinovirus $q \sim 4$ quanta/hr. $t = 25$ hr.

$$\bar{f}_c = \frac{1}{4/\text{hr}(25\text{hr})} = \frac{1}{100} = 0.01$$ } Critical re-breathed fraction $< 1\%$.

Recall $f = \dfrac{C-C_o}{C_a}$ $\quad 0.01 = \dfrac{C-C_o}{0.038}$ $\quad \therefore (C-C_o) < 0.01 \times 0.038$

$(C-C_o) < 3.8 \times 10^{-4} = 380$ ppm.

Must have $C-C_o < 380$ ppm to minimize spread (< 700 ppm ASHRAE).

SUMMARY OF KEY EQUATIONS

$$P = \frac{D}{S} = 1 - e^{-\bar{\mu}} \qquad \bar{\mu} = p_b t \bar{N}$$

$$P = 1 - \exp\left\{\frac{-I q p_b t}{Q}\left(1 - \frac{1}{\lambda\theta}\left[1 - \exp(-\lambda\theta)\right]\right)\right\}$$

$$P = 1 - \exp\left\{\frac{-I q p_b t}{Q}\right\} \qquad \text{Requires } Q.$$

} Wells-Riley Equations

$$f = \frac{\forall_e}{\forall} = \frac{C - C_0}{C_a} \qquad \text{(Re-breathed fraction)}$$

$$P = 1 - \exp\left(\frac{-\bar{f} I q t}{n}\right) \qquad \text{Requires } \bar{f}$$

Rudnick-Milton Equation.

$$D = R_{A0} = (n-1)\left\{1 - \exp\left(\frac{-\bar{f} q t}{n}\right)\right\}$$

Reproductive # in a building environment

$$\bar{f}_c = \frac{1}{qt} \ln\left\{\frac{n-1}{n-2}\right\}^n$$

Critical re-breathed fraction (to keep $R_{A0} < 1$)

Values of q (quanta/hr)

* Rhinovirus-16 ~ 1–10
* Pulmonary tuberculosis ~ 1–10
* Influenza ~ 100 (order of) / $\bar{x}$ = 67/hr (Liao et al.)
* Measles ~ 570
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