## APS COVID Webinar: October 21, 2020

### *What we know and don't know about the role of droplets and aerosol transmission of SARS-CoV-2*

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- Work was prompted by (1) a former post-doc of Dr. Bax in Wuhan who noticed that there was no coughing and sneezing going on, but people were still getting sick, and (2) a linguist who noticed that no one was talking about speech particles or studying their role in transmission.
- Dr. Musher: Once infection starts in the URT (upper respiratory track), the race is on between the virus to descend into the LRT and ramping up the adaptive immune system
- Captured speech particle droplets (from laser experiments) of different people talking, and show that we all release particles when we talk
    - Showed that a simple paper towel or wash cloth can stop most of the droplets, at least the larger ones
- Speculative conclusions:
    - Breath and speech particles are far more numerous than assumed
    - Most speech droplets stay airborne for minutes, not hours
    - Indoors there is no safe physical distance
    - Nose breathing is safer than mouth breathing
    - Droplet dehydration kinetics are complex
        - Liquid-liquid phase separation may play a role
        - Infectivity may depend on humidity
    - COVID-19 is two diseases: URT and LRT-COVID19
    - Self-infection through droplets may play a role in URT->LRT
    - Physics could bring a lot to medicine!
- Basic facts about SARS-CoV-2
    - Spike protein reacts with a receptor protein, takes about 10 minutes to enter the cell
    - Takes about 10 hours to start reproducing, creates about 10^3 virions total in the next 24-48 hr before the host cell dies
    - Saliva (sputum) contains 10^5-10^10 RNAs/mL
    - The virus exits the mouth embedded in a heap of muck, has no 'wings' to move itself
    - 10^-3 fL -> 10^15 virions/mL (if packed tightly)
        - But typical 10^5-10^10 virions/mL
    - Tiny particles (~100 nm) in a micron diameter droplet: the mass fraction of virus in a droplet is very low
    - Correct viral packaging is critical to its infectivity
        - The wrapping of the nucleic acid inside the virus is very important
        - Amount of virus in saliva drops rather slowly after a person is infected
            - But in 5-7 days, there is no culturable virus in the sputum
            - Hypothesis: this could be related to incorrect packaging of the virus
    - Mucociliary barrier provides the first defense against respiratory pathogens

        - Cilia typically move the mucus away, but virus can cluster on these cilia and sneak in (shown on SEM image)
- Hypothesized that speech droplets were the main culprits of transmission (rather than breath)
- Simple experiment with concentrated food dye showed that farthest speech droplet visible on the table by naked eye was 2.5 feet away; most droplets don't go far and remain airborne, so don't land on the table
- Laser experiment: quantify flash count as someone speaks
    - Show a distinct difference when wearing a mask
    - Also show that the baseline increases with time, due to the droplets staying airborne
- Speech droplet generation:
    - Sound generation by the vocal folds: 4 muscles modulate the airstream to create different sounds
        - Maximum glottal jet velocity = 15-45 m/s
        - Ranges from Reynolds to turbulent flow!
    - "gel-on-brush" model of respiratory mucus
    - A double liquid layer covers human airways
- Breathing droplets are generated by a different mechanism:
    - Breakup of transient occlusion in small airways
    - Evaporation of synthetic and saliva droplets shown on hydrophobic surface
        - Shows that in the absence of a phosphor-lipid, they dry out very quickly
        - Suggests that this might be related to phase separation
        - Fluorescently tagged droplets with and without DPPC shows this same dehydration
- Droplet science is very old
    - Large droplets were well quantified ~100 years ago, but missed the smaller ones
    - Aerosol research now focuses much more on small particles
- Airborne lifetime of small speech droplets experiment
    - Observed that the smaller particles have a longer time constant for decay
- Experiment with better laser showed that breathing droplets are much smaller, but very numerous and easiest observed prior to dehydration shrinkage
    - Laser light sheet is 2mm width by 8 cm height; 4W CW optical power; not an incredibly high powered laser
    - Many are small enough to pass through a cloth mask
    - "Ah" sound showed a mixture of breathing droplets and larger speech droplets (flashes)
    - Video of droplets under high humidity conditions shows that after 5 minutes, the box is even filled with small floating droplets
        - Measure terminal velocity vs scattering intensity – scaled relatively linearly
    - Under lower humidity conditions, very few breathing particles visible at all (just flashes of larger speech particles)
- High speed camera video shows how different letter sounds (speaking the notes of a scale) create different amounts of droplets, which hang around for minutes
- Several groups doing quantitative mask testing with a various exhaled breath and speech collection systems
- Is there an infectious threshold?

    - Many bacterial pathogens result in infection if the immune system gets overwhelmed
    - Respiratory virus comes in units of 1 (and many are incorrectly packaged) and landing sites are far apart
    - The probability of a virus entering a host cell and crating 1000 progeny is low (~0.01-1%)
- Dose response is typically shown on a log scale – hypothesize that this is why many people are hung up on the threshold model
- Why does higher dose correlate with more severe disease?
    - More virus exposure leads to a higher probability of getting infected directly into the lungs (lower RT)
    - Micro-aspiration is held responsible for migration from URT to LRT
        - Studied in sleep aspiration
        - People who suffer from aspiration pneumonia are shown to be much more likely to show aspiration than normal controls
    - Could self-infection through inhaled speech droplets cause migration from upper to lower airways?
        - Masks will help prevent this!

**Q&A:**

- What kind of laser do you use and how small of particles can you measure?
    - IPhone allows you to see particles down to ~ a couple of microns
    - Sony camera approaches the limit (4 Watt, 452 nm blue laser) down to ~0.5 microns
        - Can see smaller by increasing shutter time, but exposes more junk in the air!
- Can you be sure you are seeing particles coming from a person, or water vapor condensing on particles already in the air?
    - Air is very strongly filtered in the experiment box
    - Made sure the particle content in the box was very low before starting
    - The humidity controls also suggests that this is very unlikely
- What is distinction between droplets and aerosols?
    - Should consider all aerosols from a medical perspective
- What would happen if we did this experiment outdoors?
    - Once in the air, the droplets will move like smoke
    - So if you are standing right next to someone, you will get hit, but otherwise it will rapidly dilute
- Is it known if the droplets are electrically charged?
    - Not known for sure… often when you create particles with surface tension like this, they will have a variety of charges (but not known for this specific case)
- What is your general take about masks?
    - Masks are incredibly effective at blocking emission of droplets
    - Probably not very effective against inhaling droplets – maybe protect 50%
    - If we all wore masks, we could stop the transmission!
- What are your thoughts about using commercial air filters to clean the air?
    - Air purifier could do a great deal to help, but you are competing with air turnover

    - Works well as long as the size of the purifier is proportional to the size of the room
        - Needs to be pretty large (and these are pretty expensive)
    - Makeshift air filters are working well! See Jose-Luis's website
- Should the '6ft' recommendation include a 3rd dimension?
    - Use a CO2 monitor to show how much of other people's air you are breathing
    - So yes, there probably should be a volume component to social distancing
    - If people are only breathing, this is not as big of a problem, but activity and speech creates much bigger problems
        - Exercise class might be more risky too since you are inhaling deeply through the lungs, not the nose
    - Looking at superspreading events, many have happened in choirs or bars, but not in libraries or movie theaters – suggests the speech spread is much higher than breathing spread
- Is there an understanding of a minimum infection threshold?
    - There is no threshold for a highly infectious particle when dealing with a susceptible host; based on probability. Like buying a lottery ticket!
- Do some languages emit more particles than others?
    - Not much difference in actual speech mechanisms, but cultural nature of speech in different languages or regions might have differences (i.e. everyone yells in NY)
- Is there any recommendation in terms of which particles are stoppable
    - Not making official recommendations! But experimentally, most types of mask are extremely effective at stopping most particles (>90%)
    - Note that the fitting of your mask is very important! More important than the material of the mask
        - Haven't measured what escapes the sides of a mask
- How much difference does the nose make?
    - The nose actually offers a very effective filtering system
    - Nose-breathing is much safer than mouth
- Does wearing a mask make it more likely that you will move from URT to LRT?
    - No, self-infection has not been measured in these cases
    - The droplets you are producing from your vocal folds that will get trapped in your mask are too large to get back into your lungs if you breathe them back in