Synthesis of CQ1

CQ1: What Size Droplets/Aerosols Are Generated by People and How Do They Spread in Air?

Session Chair: Kimberly Prather, Scripps Institution of Oceanography, UC San Diego

1. What are the number and size of respiratory droplets/aerosols generated by individuals? Where in the respiratory tract are they generated? How do these vary by activity (e.g., speaking, coughing, singing)? How do these vary by individual?
2. How much virus is in different size droplets/aerosols? From where in the respiratory tract does virus originate? How does this vary by symptoms (including asymptomatic) and stage of infection? How does this vary by individual (i.e. superspreaders)? What leads to the variability?
3. How far do they travel in air?

(1) Inconsistent use of terminology has led to confusion for scientists, public health community, and the public

WHAT WE KNOW

- Aerosols, droplets, particles, etc. mean different things to different communities (Aerosols = stable suspension of solid/liquid particles in air)
- Cut point at 5 µm does not correspond to break in aerosol/droplet size modes, how far aerosols/droplets can travel, or whether exposure occurs by spray droplet impact or aerosol inhalation (i.e. squirt gun vs smoke)
- A more appropriate break point would be >100 µm, as it separates smaller aerosols that can float in the air for hours, travel long distances, and be inhaled from larger droplets that settle quickly

WHAT IS NEEDED

- Define transmission by exposure path
  - LARGE DROPLETS are sprayed onto the body and settle quickly
  - AEROSOLS are inhaled into the respiratory system
- Distinction according to exposure path drives:
  - Control strategies, dose response, severity of disease

(2) Individuals generate particles across a wide range of sizes and concentrations, from 100's-1000's of small aerosols to a few large droplets

WHAT WE KNOW

- Aerosols/droplets are produced across a continuum of sizes in each breath
- Size distribution is multimodal, reflecting the origin of particles in different regions of the respiratory tract which are produced via different mechanisms
- Key: A large fraction of transmission of SARS-CoV-2 involves asymptomatic individuals who are not coughing or sneezing, so they produce ~100-1000x more aerosols (i.e. small particles) than large droplets (>100 µm) through continuous breathing, talking, and singing

WHAT IS NEEDED

- Better understanding of production mechanisms and fluid composition, that lead to different sizes and numbers to explain variability
- Studies to address the fraction of droplets/aerosols that contain one or more virions, as a function of droplet/aerosol size
- Standardization of methodology/reporting/terminology to allow better synthesis across studies and to enable more clear public messaging
- The role of resuspended virus-contaminated dust and particulates is an open question

(3) Aerosol production varies widely for different people and activities

WHAT WE KNOW

- Some individuals (i.e. superspreaders) generate many more aerosols than others (COVID-19; ~10% lead to ~80% of infection)
- Louder talking and certain types of articulations produce more aerosol
- Activities that involve deeper breathing (e.g., singing, heavy exercise) produce more aerosols from the lower respiratory tract
- Speaking/singing generates more aerosols from larynx region

WHAT IS NEEDED

- Studies on how stage/location of infection, asymptomatics, fluid properties (i.e. viscosity), geometry of respiratory tract affect variability in concentrations and size distributions
- Measurements of aerosol/droplet size distributions generated by a large number of individuals at different stages of infection, asymptomatic/symptomatic during different activities
- Studies which address the amount of virus in aerosols/droplets (as a function of size) generated by many people and activities (Critical question: How is viral load distributed between different aerosol/droplet sizes?)

(4) Aerosols represent an important transmission pathway for SARS-CoV-2

WHAT WE KNOW

- Aerosols can contain infectious SARS-CoV-2 virus, remain suspended in air for hours, and be transported many meters from the source
- Asymptomatic individuals emit mostly aerosols < 10 µm and produce very few large (>100 µm) droplets
- Superspreading events are more readily explained by aerosol transmission
- Aerosols are more concentrated at close range and can spread and accumulate in a room, leading to both close and long range exposure
- Huge reduction in transmission outdoors vs indoors supports aerosol transmission

WHAT IS NEEDED

- Better ways to sample and detect infectious virus in air, in particular, methods that can sample different sizes and large volumes of air that do not damage the virus.
- Measurements of which aerosols/droplets contain viruses, i.e. are viruses enriched in small particles, concentrations, and size vary by activity, and stage of infection.
- Studies to determine the importance of transmission by viruses that are suspended into the air from surfaces
- Research is needed to determine the relative contributions of large droplets vs aerosols to transmission of SARS-CoV-2 under different environmental conditions.

(5) Multiple transmission pathways for SARS-CoV-2 can occur, supporting need for layered interventions.

WHAT WE KNOW

- Masks limit bidirectional transfer of infectious particles protecting the wearer and those surrounding the wearer
- Ventilation and filtration can have a major effect on aerosol concentrations; far fewer cases of outdoor transmission – both provide strong evidence of aerosols as transmission route
- Plexiglass barriers and face shields reduce droplet transmission, but do not limit small aerosols that are transported in the air currents
- Infectious particles on the floor, surfaces, clothing, etc. can be resuspended in air if disturbed, with implications for cleaning protocols and handling of used PPE
- Given the large spread of SARS-CoV-2 by asymptomatic hosts, the aerosol route is especially important in conversation at close distances and in crowded, poorly ventilated rooms.
- Evidence on aerosol generation, sizes, and concentrations indicates:
  - universal masking and ventilation/filtration will reduce airborne concentrations of SARS-CoV-2.
  - indoor activities should be limited and masks should be worn and distances maintained at all times indoors when multiple people are present.

Synthesis of CQ2

CQ2: Which Size Droplets/Aerosols Are Infectious and for How Long?

Session Chair: John-Martin Lowe, University of Nebraska Medical Center

1. Are smaller particles infectious?
2. How long do they remain infectious?
3. How do environmental conditions (e.g., humidity, sun) affect virus infectivity?
4. How well does masking protect the wearer and protect others from smaller particles?

(1) Humans infected with SARS-CoV-2 can produce infectious fine mode particles that may be able to transmit the disease after exposure to enough particles.

WHAT WE KNOW

- Hospital rooms show widespread contamination indicating aerosols may be involved (distance, ventilation)
- Asymptomatic and presymptomatic people are known to spread the virus, indicating the smaller aerosols produced only during breathing and speaking may carry the virus
- Aerosols < 4 μm (even < 1 μm) have been shown to contain viral RNA
- Aerosols from patient rooms have been cultured in Vero cells, and samples isolated from < 1 μm aerosol have demonstrated replication in cell culture
- Animal models (ferrets) have been shown to transmit virus through aerosol

WHAT IS NEEDED

- Characterize human generation of infectious SARS-CoV-2 aerosol
  - Variability in production rate of infectious aerosol from person to person (superspreader)
  - Production of infectious aerosol over the course of illness, severity of disease, asymptomatic/symptomatic
  - DOSE RESPONSE of SARS-CoV-2 through the aerosol route
- Aerosol collection devices that optimize preservation of intact virus

(2) Viral half-life in aerosol is approximately 1.1 hours, but can last much longer.

WHAT WE KNOW

- In a contained environment (Goldberg drum), half-life of the virus in aerosol is 1.1 hours and even after 3 hours, there are still 102 TCID50s. At 16 hours in the drum, there are still infectious viruses
- With simulated saliva vs. cell culture media, infectious aerosols are less stable

WHAT IS NEEDED

- Better understanding of human generated aerosols in environments
- Impacts of built environmental factors on virus and aerosol stability
- Characterize environmental factors for high-risk settings (long term care, meat packing plants, dental, ships, bars and restaurants, schools)

(3) UV greatly decreases virus stability, and lower temperatures and humidity may increase stability.

WHAT WE KNOW

- UV rapidly inactivates SARS-CoV-2 in aerosols
- SARS-CoV-2 infectivity declines slowly in aerosols at room temperature
- Relative humidity had a small effect on infectivity in aerosols, with higher humidity resulting in lower infectivity

WHAT IS NEEDED

- Effect of low temperatures on stability in aerosols
- Stability in aerosols made of relevant liquid (i.e. respiratory secretions)
- Changes in aerosol composition during disease could affect stability of SARS-CoV-2 in those aerosol
- Experiments using aerosolized virus in appropriate liquid evaluating broad range of temperature/humidity/sunlight.

(4) Available evidence for face coverings (masks) consistently indicates a reduction of community transmission.

WHAT WE KNOW

- There is mechanistic evidence that face masks provide source control of virus-laden droplets and aerosols.
- Mechanistic evidence face masks provide protection for the wearer.
- Meta-analysis found limited number of studies on effectiveness of community face covering strategies. Studies of both masks and hand hygiene demonstrate reduction in community transmission

WHAT IS NEEDED

- Define the characteristics of an improved/optimal face covering to support source control
- Develop greater understanding of effective community face covering strategies (public transit, prolonged use, indoor congregate settings) to inform clear public guidance

Synthesis of CQ3:

CQ3: What behavioral and environmental factors determine personal exposure to SARS-CoV-2?

Session Chair: John Volckens, Colorado State University

1. What human behaviors increase risk of exposure?
2. Does droplet/aerosol size influence personal exposure and intake?
3. What role does the built environment play in determining exposure risk?
4. How does the built environment contribute to risk from super-spreader events?
5. What is the role of masks and face shields in mitigating exposure risk?

(1) Short- and long-range modes of airborne transmission/exposure are important indoors.

WHAT WE KNOW

- **Short-range (<1.5 m)**: large drops AND aerosol < 100 µm present in respiratory plumes
  - ***Sharing of respiratory plumes*** modulated by distance, behavior, local turbulence, posture, etc..
  - "Typical" room ventilation is unlikely to reduce exposure to shared respiratory plumes
  - Masks (face coverings) reduce aerosol emissions at the source by ~50-90%
  - Masks reduce intake of aerosol by ~25-90%
  - Masks reduce jet propagation of the respiratory plume
- **Long-range (>1.5 m)**: smaller (persistent) aerosol dominates exposure
  - Masks reduce both emissions and intake of drops & aerosol by wearer
  - Room ventilation/filtration can reduce exposure
  - Higher ventilation rates (delivery of clean air) are better to reduce risk of exposure

WHAT IS NEEDED

- Flexible, scalable models to improve understanding of the complexity and dynamic nature of exposure (e.g., to help determine how much airflow is "enough").
- Comprehensive data on human bioaerosol emissions (variation by individual, time, activity) and exposures.
- Improved exposure measurement technology (personal, spatial & temporal variability, size-resolved, supports viability) to define timing, location, mode, and intensity of exposure.

(2) Indoor environments are a common feature among superspreading events.

WHAT WE KNOW

- Documented super-spreading events supported by presence of crowds, confinement, close contact, continuous exposure.
- Layered approaches to interventions (spacing, ventilation, filtration, masks) are known to reduce aerosol exposures in built environment. Models suggest factors of 2-5 reduction in infection risk.
- Individual behaviors are a major determinant of exposure risk.

WHAT IS NEEDED

- Research on surveillance and exposure reduction: preventing super-spreading events before they happen.
- Interdisciplinary research that demonstrates effective ways to reduce emissions, exposure risks: a wicked problem spans physical AND social sciences.

(3) Ventilation, filtration, and germicidal UV practices can reduce room-based exposure (long-range), if applied correctly

WHAT WE KNOW

- Ventilation should be based on occupancy (L/person/s) but there is no “one size fits all” rate to eliminate exposure risk.
- Filtration is an effective supplement to ventilation for reducing aerosol concentrations indoors. CADR must be sized to occupancy, room volume, existing ventilation.
- Germicidal UV damages DNA/RNA and can be useful in environments where it is otherwise challenging to ventilate/filter, there is potential for infectious particles, and if used in a way that doesn't expose people to UV radiation (e.g., in upper air).
- Control at the emission source is more effective than control of the environment.

WHAT IS NEEDED

- Quantitative evidence of infection risk reduction as a function of applied control technology.
- Energy-efficient and cost-effective technologies and strategies to promote removal and inactivation of SARS-CoV-2 in existing building and housing stock.

Synthesis of CQ4:

CQ4: What Do We Know about the Infectious Dose and Disease Relationship for SARS-CoV-2?

Session Chair: Seema Lakdawala, University of Pittsburgh

1. Can people inhale enough to be infected? How much does risk of being infected depend on inhaled dose?
2. Is clinical phenotype related to dose?
3. What are the biological modifiers of the dose-response relationship (age, sex, underlying conditions)?

(1) Acquisition of SARS-Cov-2 infection through air in animals

WHAT WE KNOW

- Valuable animal models to examine SARS-CoV-2 transmission both by direct and aerosol routes.
- Animals infected with SARS-CoV-2 can release virus-laden aerosols that can infect susceptible recipients.
- Transmission occurred early after infection and not late.
- For influenza viruses, expelled aerosols showed contained more virus in larger sizes compared to smaller aerosols.
- Transmissibility of aerosols was dependent upon size.

WHAT IS NEEDED

- Utilize aerosol inoculation systems to define infectious dose response models for SARS-CoV-2.
- Study how transmission of SARS-CoV-2 varies with aerosol/droplet size.
- Size distribution of virus-laden airborne particles in the exhaled breath of SARS-CoV-2 infected animals.
- Infection initiation site of virus-laden aerosols.

(2) Infectious dose and disease severity are linked

WHAT WE KNOW

- Animal studies with SARS-CoV suggest that higher inoculum dose will lead to more severe infection.

WHAT IS NEEDED

- Research on risk of repeated exposures, using animal models
- Experimental aerosolization studies of traceable (i.e., luciferase) to track in real time deposition site and disease severity within a single animal.
- Need to use a natural infection approach in animals models and if that makes a difference.

(3) Age, sex, and health status impact disease severity

WHAT WE KNOW

- Similar doses can result in different disease outcomes based on age, genetics and obesity.
- In genetically similar mice, age significantly increases severity independent of viral replication.
- Males and females have distinct case fatality rates and males may shed more virus.
- Potential mechanisms include difference in virus receptors, virus sensing, and innate and adaptive immune response.

WHAT IS NEEDED

- Controlled experimental studies on animals with different age ranges and sexes.
- Combinations of underlying health issues/sex/age
- Epidemiology data broken up by sex and age to determine transmission risk and infection rates.