ISAM webinar – July 20, 2020

Breathing is enough – Spread of SARS-CoV-2 via Aerosols and the Consequences for Infection Control

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Overview

➢ Aerosol

➢ A Small History of Exhaled Aerosols

➢ SARS-COV-2 as an Aerosol?

➢ Consequences?
Aerosol?
Aerosol

An Aerosol is a **Suspension** (a mixture) of fine solid particles or liquid droplets in air or another gas.

Aerosol particles are the fine solid particles or liquid droplets.

The aerosol particles must stay in the gas for more than a few seconds. Otherwise we are not talking about aerosol (Example: Fog = Aerosol; Rain ≠ Aerosol). There is no upper size limit.

A particle (water droplet) of 10 µm need 6 min to fall to the ground from 1 m high.

There is no 5 µm limit! And a droplet nuclei is not an Aerosol! It might be an aerosol particle!
Deposition in the Respiratory Tract

- Particle size
- Shape
- Electrical charge
- Hygroscopicity

Deposited

Exhaled

Intrathoracic Deposition

Particle Diameter, µm

Deposition

0,001 0,01 0,1 1 10 100

5 µm
History

1986

In an experimental setup with a strong and very sensitive laser photometer we found that during quiet normal breathing of healthy volunteers the lung generated aerosol particles:

1.) The origin of these particles was in the deep lung.

2.) On average they were about 0.4 µm median diameter.

3.) A breathhold could reduce the number of exhaled particles, flow rate did not change concentration significantly.

4.) With an RV (residual volume) breathing manouevre the concentration increased significantly.

5.) We found huge differences between subjects, concentration between one and several thousand particles per litre of exhaled air.

6.) One day before one of our subjects got sick (airway infection) the concentration went up by several orders of magnitude.
Our Conclusions:

1.) The particles were not generated by shear forces. These particles are generated during inhalation and it might be that reopening of collapsed small airways was responsible for this findings.
Droplet formation

Droplet particles (an aerosol) are formed through rupture of RLF film during airway re-opening.

Reproduced with minor modification with permission from Per Larsson, Sahlgrenska Academy, University of Gothenburg, Sweden and PExA AB
Our Conclusions:

1.) The particles were not generated by sheer forces. These particles are generated during inhalation and it might be that reopening of collapsed small airways was responsible for this findings.

2.) An increased production of surfactant or mucus could increase the exhaled respiratory droplets.

Other research groups have now confirmed our findings. Katharina Schwarz and Jens Hohlfeld from Hannover, Johnson and Morawska as well as the group around Anna-Carin Olin from Gothenburg, Sweden.
Intersubject variability of exhaled particles

Almstrand AC, Bake B, Ljungström E, et al. Effect of airway opening on production of exhaled particles. J Appl Physiol (2010). 2010;108(3):584-588
Intrasubject variability

Kokelj S, Kim JL, Andersson M, Runström Eden G, Bake B, Olin AC. Intra-individual variation of particles in exhaled air and of the contents of Surfactant protein A and albumin. PLoS One. 2020;15(1)
Inhalation of isotonic saline reduced significantly the generation of the exhaled particles.

Inhalation of surfactant increased the production.

Edwards DA, Man JC, Brand P, et al. Inhaling to mitigate exhaled bioaerosols. Proc Natl Acad Sci U S A. 2004;101(50):17383-17388. doi:10.1073/pnas.0408159101
Do these exhaled particles contain viruses?

Patricia Fabian first showed that in a limited number of patients.

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Fabian P, McDevitt JJ, DeHaan WH, et al. Influenza virus in human exhaled breath: An observational study. PLoS One. 2008. doi:10.1371/journal.pone.0002691
Do these exhaled particles contain viruses?

Donald Milton and colleagues measured the virus RNA in 37 influenza patients.

In the larger size fraction, generated by cough and speaking they found in **16 of 37 Patients** Virus RNA. In the fraction < 5µm they found in **34 of 37 Patients** Virus RNA.

They also measured the 'Culturability‘ of the viruses in these droplets:

Milton DK, Fabian MP, Cowling BJ, Grantham ML, McDevitt JJ. Influenza Virus Aerosols in Human Exhaled Breath: Particle Size, Culturability, and Effect of Surgical Masks. PLoS Pathog. 2013;9(3). doi:10.1371/journal.ppat.1003205
Viruse in Exhaled Breaths

Milton DK, Fabian MP, Cowling BJ, Grantham ML, McDevitt JJ. Influenza Virus Aerosols in Human Exhaled Breath: Particle Size, Culturability, and Effect of Surgical Masks. PLoS Pathog. 2013;9(3). doi:10.1371/journal.ppat.1003205
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Median number for particles > 5 µm = 0 Copies, for particles < 5 µm = 110 copies. 'Fine particles contained 8.8 (95% CI 4.1 to 19) fold more viral copies than did coarse particles'.
Do these exhaled particles contain viruses?

David Lindsley published data in 2016 that he found viable Influenza A viruses in air samples. He investigated 53 subjects with influenza A. In 53% he found virus in particles generated by cough and in 43% in particles generated by breathing only.

His conclusion:

‘Viable influenza A virus was detected more often in cough aerosol particles than in exhalation aerosol particles, but the difference was not large. Because individuals breathe much more often than they cough, these results suggest that breathing may generate more airborne infectious material than coughing over time. ..... Our results are also consistent with the theory that much of the aerosol containing viable influenza originates deep in the lungs.’

Lindsley WG, Blachere FM, Beezhold DH, et al. Viable influenza A virus in airborne particles expelled during coughs versus exhalations. Influenza Other Respir Viruses. 2016;10(5):404-413
What do we know about SARS CoV 2 viruses?

SARS-CoV-2 virus use ACE2 receptors

Reproduced with minor modifications from Anna Bredberg Sahlgrenska Academy, University of Gothenburg, Sweden and Ni W, Yang X, Yang D, et al. Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. Crit Care. 2020;24(1):422. Published 2020 Jul 13. doi:10.1186/s13054-020-03120-0
SARS-CoV-2 and Aerosol?

Bae and coworkers found in 4 patients with COVID 19 that virus particles could be detected in petri dishes in front of patients despite the fact that they were wearing facemasks. And they published that no viruses could be detected on the inner surface but at the outside of the masks.

Meanwhile the publication was restracted because some of the measurements were below the official detection limit of the measuring device.

Bae, Seongman et al. “Effectiveness of Surgical and Cotton Masks in Blocking SARS-CoV-2: A Controlled Comparison in 4 Patients.” Annals of internal medicine vol. 173,1 (2020)
Transmission of SARS-COV 2 as aerosol?

April 2: COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China

Li Y, Qian H, Hang J, et al. Evidence for probable aerosol transmission of SARS-CoV-2 in a poorly ventilated restaurant. medRxiv. 2020:2020.04.16.20067728. doi:10.1101/2020.04.16.20067728
Transmission of SARS-COV 2 as aerosol?

March 19: Van Doremalen und coworkers showed that SARS COV 2 Viruses survived over several hours in an aerosol when sprayed into a closed non ventilated room.

April 7: Quian and coworkers found in more than 7.000 infections just one single transmission outside a room: ‘….the corona COVID-19 infection is an indoor phenomenon’ and almost no infections occur outside....

April 10: Lidia Morawska and Junji Cao wrote: Airborne transmission of SARS-CoV-2: The world should face the reality!

van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med. 2020. doi:10.1056/NEJMc2004973

Quian H, Miao T, Liu L, Zheng X, Lu D, Li Y. Indoor transmission of SARS-CoV-2. https://www.medrxiv.org/content/medrxiv/early/2020/04/07/2020.04.04.20053058.full.pdf.

Morawska, Lidia, and Junji Cao. “Airborne transmission of SARS-CoV-2: The world should face the reality.” Environment international vol. 139 (2020): 105730. doi:10.1016/j.envint.2020.105730
Transmission of SARS-COV 2 as aerosol?

April 27: Liu and colleague took aerosol samples in a Wuhan hospital. They found in several of these samples SARS-COV-2 Viruses. In a protective apparel removing room they found most of the viruses in the particle fraction between 0.25-0.5µm.

Liu Y, Ning Z, Chen Y, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals [published online ahead of print, 2020 Apr 27]. Nature. 2020;10.1038/s41586-020-2271-3. doi:10.1038/s41586-020-2271-3
Transmission of SARS-COV 2 as aerosol?

May 15: Attack Rate Following Exposure at a Choir Practice Skagit County, Washington
Confirmed and probable cases of COVID-19 associated with two choir practices, by date of symptom onset (N = 53) — Skagit County, Washington, March 2020

Hamner L, Dubbel P, Capron I, et al. High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice - Skagit County, Washington, March 2020. MMWR Morb Mortal Wkly Rep. 2020;69(19):606-610. Published 2020 May 15
Transmission of SARS-COV 2 as aerosol?

June 3: Santarpia and colleagues from the University of Nebraska took air samples in a hospital and found SARS-CoV-2 viruses even in samples in a hallway outside of the patients room.

And they found positive air samples even in the absence of cough of the patients.

Santarpia JL, Rivera DN, Herrera VL, et al. Aerosol and surface Transmission Potential of SARS-CoV-2
https://doi.org/10.1101/2020.03.23.20039446.
Transmission of SARS-COV 2 as aerosol?

July 8: SARS-CoV-2 is transmitted via contact and via the air between ferrets.

SARS-CoV-2 was transmitted via the air to three out of four indirect recipient ferrets. This study provides experimental evidence of robust transmission of SARS-CoV-2 via the air!

Richard M, Kok A, de Meulder D, et al. SARS-CoV-2 is transmitted via contact and via the air between ferrets. Nat Commun. 2020;11(1):3496. Published 2020 Jul 8. doi:10.1038/s41467-020-17367-2
Transmission of SARS-COV 2 as aerosol?

- Yes, there is sufficient evidence to believe that the aerosol route is an important transmission factor in the recent COVID19 pandemic.

- My feeling is: There are two ports of entry for SARS-CoV-2:
  - Nose
    - If this is the main infection site, the disease will be mild.
  - Alveolar Region
    - If infected via tiny aerosol particles in this region, disease can be severe

- Aerosol particles can be generated by breathing, speaking, singing, coughing, sneezing. A distinction between droplets and aerosol is not needed. If particles in the air are inhaled: it is an aerosol infection.
Protection against exhaled virus aerosols

Limit Number of Contacts in a Room (no Parties, no choir practice, closed restaurants, closed schools, ....)

Face Masks

Airfiltration

Reduce concentration of exhaled particles

Other measures
Meta-analysis of randomized controlled trials (RCTs) indicated a protective effect of masks and respirators against clinical respiratory illness (CRI) (risk ratio [RR] = 0.59; 95% confidence interval [CI]:0.46–0.77) and influenza-like illness (ILI) (RR = 0.34; 95% CI:0.14–0.82).

‘Our analysis confirms the effectiveness of medical masks and respirators against SARS. Disposable, cotton, or paper masks are not recommended.’
Renyi Zhang and colleagues found that wearing face masks had an effect on the distribution of SARS-CoV-2 pandemic. "We conclude that wearing of face masks in public corresponds to the most effective means to prevent interhuman transmission, ....in conjunction with simultaneous social distancing, quarantine, and contact tracing, represents the most likely fighting opportunity to stop the COVID-1.

Mask? Pro

A

Social distancing

Stay-at-home

Face-covering

NYC

B

Social distancing

Stay-at-home

U.S.

Date

Mar. 1
Mar. 15
Mar. 29
Apr. 12
Apr. 26
May 10

Daily new confirmed cases (in 10^4)

y = -39x + 5078

y = -106x + 3304

y = 70x + 21207

Zhang, R., Li, Y., Zhang, A. L., Wang, Y., & Molina, M. J. (2020). Identifying airborne transmission as the dominant route for the spread of COVID-19. Proceedings of the National Academy of Sciences, 202009637. https://doi.org/10.1073/pnas.2009637117
Face Mask? CON

MacIntyre, 2009 tested wearing of surgical masks, P2 (FFP2) mask and no mask in a controlled study.

Outcome:

ILI (Influenza like illness) was reported in 21/94 (22.3%) in the surgical group, 14/92 (15.2%) in the P2 group, and 16/100 (16.0%) in the control group.

We concluded that household use of face masks is associated with low adherence and is ineffective for controlling seasonal respiratory disease.

MacIntyre CR, Cauchemez S, Dwyer DE, et al. Face mask use and control of respiratory virus transmission in households. Emerg Infect Dis. 2009;15(2):233-241. doi:10.3201/eid1502.081167
Face Mask?   CON

1607 healthcare workers were randomized in 3 groups: 1.) wearing no masks; 2.) wear a cloth mask 3.) wear a surgical mask

Figure 2  Outcomes in trial arms (CRI, clinical respiratory illness; ILI, influenza-like illness; Virus, laboratory-confirmed viruses).
Face Mask: Conclusion

- The use of **Surgical Face Masks** can be strongly recommended

- The use of **Cloth Face Masks** is questionable:

  ‘...The filtration effectiveness of cloth masks is generally lower than that of medical masks and respirators; however, cloth masks may provide some protection if well designed and used correctly. ...... Until a cloth mask design is proven to be equally effective as a medical or N95 mask, wearing cloth masks should not be mandated for healthcare workers. In community settings, however, cloth masks may be used to prevent community spread of infections by sick or asymptomatically infected persons, and the public should be educated about their correct use.

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Chughtai AA, Seale H, Macintyre CR. Effectiveness of Cloth Masks for Protection Against Severe Acute Respiratory Syndrome Coronavirus 2 [published online ahead of print, 2020 Jul 8]. Emerg Infect Dis. 2020;26(10):10.3201/eid2610.200948. doi:10.3201/eid2610.200948
Air Filtration

- One infected person
- Exhalation of 100 virus copies/Liter exhaled air
- 15 breaths/min a 1 Liter
- Room volume: 40 m³
- Time 2 hrs
- Halftime of virus in air: 125 min

Result: 132,000 virus copies after 2 hrs → 3.3 virus copies/Liter

In 10 min another person in this room will inhale 500 virus copies.
Air Filtration

Exhaled Viruses in a Room with an Infected Person

NEP (without)  NEP (with 12)  NEP (with 5)

NEP (with 12/5) = number of particles in the room with air-filter that removes 50% of particles in 12/5 min.
Air Filtration

- One infected person
- Exhalation of 100 virus copies/Liter exhaled air
- 15 breaths/min a 1 Liter
- Room volume: 40 m³
- Time 2 hrs
- Halftime of virus in air: 125 min

Result with Filtration: 20,000 virus copies after 2 hrs → 0.5 virus copies/Liter

In 10 min another person in this room will inhale only 75 virus copies.
Air Filtration

- The most efficient filtration is: opening the windows!

- If this is not feasible, airfiltration can be an alternative. With existing HEPA filters it is possible to reduce the virus burden by a factor of 5-20.
Virus inactivation by UV Light

Buonanno and colleagues showed that UV Light 222 nm, which is not harmful for human skin can inactivate Corona virus: 1.7 and 1.2 mJ/cm² inactivated 99.9% of aerosolized coronavirus 229E in 25 min.

Michael Schuit and coworkers found that simulated sunlight rapidly inactivates SARS-CoV-2 in aerosols.

Hiroko Inagaki et al. just recently published data that DUV (deep UV) light with 280 nm and 37.5 mJ/cm² resulted in 99.9% inactivation of SARS-CoV-2.

Schuit M, Ratnesar-Shumate S, Yolitz J, et al. Simulated Sunlight Rapidly Inactivates SARS-CoV-2 on Surfaces. J Infect Dis. 2020;May(274):Epub ahead of print. PMID: 32432672. doi:https://doi.org/10.1080/00498254.2020.1737890

Inagaki H, Saito akatsuki, Sugiyama H, Okabayashi T, Fujimoto S. Rapid inactivation of SARS-CoV-2 with Deep-UV LED irradiation. Prepr bioRxiv. 2020;0(0):2020.06.06.138149. doi:10.1101/2020.06.06.138149

Buonanno M, Welch D, Shuryak I, Brenner DJ. Far-UVC light (222 nm) efficiently and safely inactivates airborne human coronaviruses. Sci Rep. 2020;10(1):1-8. doi:10.1038/s41598-020-67211-2
Conclusion

It is plausible that SARS-CoV-2 will be transmitted via aerosols.

Is this the most important transmission? I don’t know.

Wearing of face masks seems a possible measure to reduce transmission.

HEPA filters are able to reduce the risk of infection in closed indoor rooms.

UV-Light might be an alternative to reduce the SARS-CoV-2 viral burden.
Thank You for your attention. DANKE.

There are some questions that can't be answered by Google.