Summary of discussion at mini-conference “Plasma-based applications to ameliorate COVID-19”

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Research and Review seminar, PPPL November 23, 2020
Mini-conference “Plasma-based applications to ameliorate COVID-19”

- November 12: TM13 8 talks; VM09 8 talks
- DPP press release is online: [Plasma-Based Technology to Fight COVID-19](#)
- Discussed
  - various plasma devices for disinfection
  - immunological mechanisms of the variability of the antibody responses
  - detecting SARS-CoV-2 in droplets by mass spectrometry and lasers
  - fluid dynamic science associated with contamination and decontamination
  - modeling of SARS-CoV-2 transmission
  - UV light disinfection of air and water.
Take-away message

• The antibody responses vary and may not be effective
• Infection transmission occurs from presymptomatic and asymptomatic for few days up to week.
• Nose breathing is much safer than mouth breathing, because Covid-19 has two very different forms: upper respiratory and low respiratory.
• Breathing and speech produces a lot of particles.
• Small droplets stay for very long time and move with air flow => ventilation design is most important factor.
• No safe distance indoors as droplets accumulate.
• UV light disinfection of air and water is the most effective
  • 254nm standard lamps are cheap but require (simple) safety protocol
  • New 222nm lamps are much safer because they can be used with people in the room
• Split system air-conditioning – recirculation in space may be a factor
• No ventilation air supply
• Four exhaust fans, none running
• Measured ventilation rate ~0.75 –1 L/s-pers
• No close contact observed on video
• Conclusion: “aerosol transmission of SARS-CoV-2 due to poor ventilation may explain the community spread of COVID-19.”

Motivation

• How many people allowed in a room, train car, lecture hall, prison? See, e.g. [CDC Reduces Consecutive Minutes Of COVID-19](https://www.cdc.gov/coronavirus/2019-ncov/community/condense-time.html)

• Is there a scientific answer?

• Answer should be somewhat quantifiable and depend on how many viruses from a potentially infected person can transmit to a healthy person above infection dose => need to look at

• Infection Transmission, Ventilation, Disinfection
What we know and don’t know about the role of droplets and aerosol in transmission of SARS-CoV-2
Speaker: Adriaan Bax, NIH

What we know and don’t know about SARS-CoV-2: origins and evolution
Speaker: Raul Rabadan

Epidemiology of COVID-19: Implications for Control
Speaker: Marc Lipsitch
A Message from TRB Executive Director Neil Pedersen Regarding TRB and COVID-19

COVID-19 has had a profound impact on both the transportation system and the transportation professional community. TRB’s first priority is, and always will be, the safety and health of the members of our stakeholder community, including our many thousands of volunteers and our dedicated staff.

RAPID EXPERT CONSULTATION

Advantages and Limitations of COVID-19 Diagnostic Tests

A new rapid expert consultation examines the advantages and trade-offs of the different types of COVID-19 tests that are currently available. It also considers testing strategies for symptomatic and asymptomatic individuals, as well as data reporting systems.

REPORT

Decarcerating Correctional Facilities during COVID-19: Advancing Health, Equity, and Safety

Correctional facilities have become hotspots for infection during the COVID-19 health crisis. Our recent report offers recommendations that call for immediate actions to facilitate decarceration efforts, improve preparedness for future COVID-19 outbreaks and the next public health crisis.

FEATURE STORY

Putting Games to Work in the Battle Against COVID-19

“Jamming the Curve” enlisted over 400 independent video game developers around the world to develop concepts for games that reflect the real-world dynamics of COVID-19. Read about the game jam and the five winning games.

Q&A: COVID-19 and Airborne Transmission

This summer, the National Academies brought together engineers, virologists, public health experts, and others for a deep dive into what is being learned about airborne transmission of COVID-19. Jonathan Samet, who helped plan the event, discusses its impact and how the research community can use a new summary of the workshop in their

VIDEO

HVAC Strategies in Response to COVID-19

What facility heating, ventilation, and air conditioning strategies are needed to prevent or mitigate the spread of COVID-19? A recent webinar explored strategies, system and facility design, and practical experience for preparing federal facilities for occupancy.
A large share of Covid infections are caused by “super-spreading” events. Super-spreading events are selected cases where more than 30 people were infected. The graphic shows that in two Indian states, 10% of people caused 60% of subsequent infections. Setting of super-spreading events show that medical, prison, and nursing home settings are the most common.
A small share of the population is responsible for a majority of infections

Cumulative share of subsequent covid-19 infections, %
India*, by percentile of subsequent infections per initial case

About 60% of subsequent infections were caused by just 10% of people

Around 70% of people who tested positive did not infect anyone else

*Study in Andhra Pradesh & Tamil Nadu, March-August 2020
Proportion of contacts with a positive test result stratified by case and contact age. Contour plots indicate the proportion of exposed contacts with a positive test result by case and contact age for all contacts.
The authors’ treasure trove of data gives clues to how those infections happen. Risk of infection is greatest in private homes and among similarly aged people. That is corroborated by evidence from 1,600 covid-19 “super-spreading” events. Such transmission occurs most often in large buildings, while just three documented events have taken place outdoors.
Basic Facts: Viral Load

Virological assessment of hospitalized patients with COVID-2019

Viral load: peak concentrations were reached before day 5, more $5 \times 10^8$ copies per swab. This suggests active virus replication in tissues of the upper respiratory tract. SARS-CoV in sputum at $1.2–2.8 \times 10^6$ copies per ml. The shedding of infectious virus in sputum continued throughout the first week of symptoms. Later in the disease, COVID-19 resembles SARS in terms of replication in the lower respiratory tract. Of note, the two patients who showed some symptoms of the lungs being affected showed a prolonged viral load in sputum. The combination of very high concentrations of virus RNA and the occasional detection of cells in stools that contain subgenomic mRNA indicate active replication in the gastrointestinal tract. Our results suggest that measures to contain viral spread should aim at droplet-, rather than fomite-, based transmission. The prolonged viral shedding in sputum is relevant not only for the control of infections in hospitals, but also for discharge management.
Some basic facts about SARS-CoV-2

![Schematic diagram of SARS-CoV-2 interaction with human cell]

**Host Cells**
- Type I & II pneumocytes (~$10^{11}$ cells)
- Alveolar macrophage (~$10^{10}$ cells)
- Mucous cell in nasal cavity (~$10^5$ cells)
- Host cell volume: $\sim 10^3 \text{ mm}^3 = 10^3 \text{ fl}$

**Concentration**
- Nasopharynx: $10^6$-$10^9$ RNAs/swab
- Throat: $10^4$-$10^8$ RNAs/swab
- Stool: $10^4$-$10^8$ RNAs/g
- Sputum: $10^6$-$10^{11}$ RNAs/mL

**Replication Timescales**
- Virion entry into cell: $\sim 10$ min (measured for SARS-CoV-1)
- Eclipse period: $\sim 10$ hrs (time to make intracellular virions)
- Burst size: $\sim 10^3$ virions (measured for MHV coronavirus)

**Global Spread**
- By the end of June, the D614G mutation was found in almost all SARS-CoV-2 samples worldwide.

Correct viral packaging is critical to its infectivity
A key role for nucleocapsid

C.-k. Chang et al. / Antiviral Research 103 (2014) 39

(B) SARS-CoV

Wolfel et al, Nature
doi.org/10.1038/s41586-020-2196-x
Mucociliary barrier providing the first defense against respiratory pathogens

- Mucus
- Serous layer
- Ciliated epithelial cells

Cell types:
- Macrophage
- Innate lymphoid cell
- Goblet cell
- T cell
- Dendritic cell
- Mast cell
- Neutrophil
CRRG Webinar: The role of droplets and aerosol in transmission of SARS-CoV-2

Scanning Electron Microscopy of SARS-CoV-2 Infected Airway Cells

mucus

virus

cilia

DOI: 10.1056/NEJMcim2023328

Adriaan Bax
Infection transmission occurs from presymptomatic and asymptomatic for few days up to week.

Nose breathing is much safer than mouth breathing, because Covid-19 has two very different forms upper respiratory and low respiratory.

Breathing and speech produces a lot of particles.

Small droplets stay for very long time and move with air.

No safe distance indoors as droplets accumulate.

Probability of virus entering host cell is low $10^{-4}$-$10^{-5}$ hence minimum infectious dose $\sim 10^5$
Small droplets stay for very long time and convect with air.
No safe distance indoors as droplets accumulate.
Probability of virus entering host cell and multiplying is low $10^{-3}$-$10^{-4}$ hence minimum infectious dose $\sim 10^5 10^3$
SARS-CoV in sputum at $1.2–2.8 \times 10^6$ copies per ml.

⇒ Inhaling 0.01-0.1 ml of infected sputum leads to infection!
⇒ Indoors: need for continuous air disinfection or fast ventilation
Review of fluid dynamic science associated with contamination and decontamination

Andrei Khodak, Igor Kaganovich, and Mikhail Shneider

Jet: 22-degree angle

https://doi.org/10.1016/j.ijmultiphaseflow.2013.02.004
Small droplets follow the surrounding fluid around the face, but large droplet deposit onto face due to inertia.

Deposition Efficiency on 0.2[m] sphere

- 0.1 [m/s]
- 1 [m/s]
- 10 [m/s]
Turbulent jet profile

Figure 9.2: Schematic description of a jet penetrating in a fluid at rest. The widening is linear with distance, and all cross-jet velocity profiles, except those very near the orifice, are similar to one another, after suitable averaging over turbulent fluctuations.

Turbulent submerged jet: Gaussian Profile \( u_{cl} = 6.2 \frac{u_0 d_{mouth}}{x} \)

Figure 9.4: Mean axial velocity versus radial distance in a turbulent round jet at Reynolds number \( Re \approx 10^5 \). The velocity is scaled by the maximum value at the center of the jet, and the radial distance by \( r_{50\%} \), the distance at which the velocity drops to half of its maximum value. (Adapted from Pope, 2000)
From unsteady exhalation to a steady jet

VM09.00001: Puff trains in speaking produce long-range turbulent jet-like transport potentially relevant to asymptomatic spreading of viruses

Howard Stone, Manouk Abkarian, Simon Mendez, Nan Xue, Fan Yang
Influence of flow signal

Residence time (s)

Breathing 1

(1.95;0.35)

Breathing 2

(1.95;0.3)

Peter Piper picked a peck

(1.8;0.32)

Sing a song of six pence

(1.8;0.35)

Same trends for all jets, but in speech: shorter and rougher jets
Droplet distribution in cough

Feng et al. Journal of Aerosol Science 147 (2020) 105585
Mask Filtration Efficiency

![Graph showing filtration efficiency of different types of masks](image)

- N95/KN95
- Surgical Mask
- Procedure Mask
- Cotton Mask
- Gauze Mask

Filtration Efficiency (%) vs. Particle Diameter (μm)
Droplet time in air

Balance of gravity and friction force give estimates of how quickly droplet falls and fall (terminal) velocity

\[ \frac{1}{6} \pi d^3 \Delta \rho g = \frac{3 \pi \mu V d}{C_c} \]

Time to fall versus droplet diameter in μm

Settling time [min] from 1.75 m height of water droplet in Air

Terminal Velocity [m/s] of water droplet in Air

Fall velocity versus droplet diameter in μm
Droplet spread in air top no mask, bottom mask is on 1 cm apart from face
Outline

- UVc use for disinfection of surfaces and air
  - The Second Gilbert W. Beebe Webinar: Safety and Efficacy of UVC to Fight COVID-19
UVc use for disinfection of surfaces and air

Covid virus ‘survives for 28 days’ in lab conditions bout room temperature, and in the dark. The flu virus can survive for 17 days (Virology Journal). It also stayed longer on smooth, non-porous surfaces than on porous materials such as cloth, which was found not to carry any infectious virus past 14 days. Though infectious viruses will only persist for hours in mucus on surfaces rather than days.=> **Instead of washing everything with chemicals in doctor’s offices and other frequented places better use UVc with safety glasses and gloves**

- UV disrupts microbial DNA/RNA, prevents reproduction
- Coronavirus susceptibility is good
- Long record of application
- CDC approved for tuberculosis control as adjunct to filtration

Federal Facilities Council Webinar: Heating, Ventilation, and Air Conditioning Strategies in Response to COVID-19
Engineering Controls for COVID-19 Aerosol Risk Mitigation
William P. Bahnfleth, PhD, PE, FASHRAE, FASME, FISIAQ Professor,
The Pennsylvania State University, USAChair, ASHRAE Epidemic Task Force
UVc use for disinfection of surfaces and air

- The Second Gilbert W. Beebe Webinar: Safety and Efficacy of UVC to Fight COVID-19
- Very long known and established technology,
- need fluence in mJ/cm² for log reduction
  
  | Infectious Hepatitis | N/A | 5.8 | 11.6 | 17.4 | 232.0 | UV-Light.co.UK  |
  | Infectious Hepatitis | N/A | 3.4 | 6.8  | 10.2 | 136.0 | UV-Light.co.UK  |
  | Influenza           | N/A | 3.4 | 6.8  | 10.2 | 136.0 | UV-Light.co.UK  |

For 1000 reduction it takes 10mJ/ cm² fluence. Typical 25W/100cm²= 2.5mJ/ cm² ($30) needs 4s exposure.

=> Instead of washing everything with chemicals in doctor’s offices and other frequented places better use Uvc for few seconds with safety glasses and gloves
UV Light Disinfection of Air and Water

Leonid Vasilyak
Joint Institute for High Temperatures of Russian Academy of Sciences, Moscow

Sergey Kostyuchenko
LIT, Moscow
www.lit-uv.com

APS-DPP 2020 Virtual Meeting
USA
November 12, 2020
OPEEN UV DISINFECTION SYSTEMS FOR AIR & SURFACE

UV system should be able to provide:
a high UV dose (25 mJ/cm²).

We recommend to use powerful mobile UV irradiators (with a total UV power of at least 200-300 W and an electric power of at least 600 W)

UV irradiator “SVETOLIT 600“
4 lamps DB500,
Total electric power - 2 000 W,
UV power - 600 W

Treatment time
Room volume 75 m³ ---- 5 minutes
200 m³ ---- 13 minutes

Slide courtesy of L. Vasilyak
UV DISINFECTION IN THE VENTILATION AND AIR CONDITIONING SYSTEM OF THE SUBWAY CAR

Slide courtesy of L. Vasilyak
UV AIR RECIRCULATOR AEROLIT 550 m³/h,
high UV dose of 30 mJ/cm²

For the disinfection of indoor air in the presence of people
(who are possible sources of continuous air contamination)

Air recirculation rate of at least 5 times per hour is required.

Slide courtesy of L. Vasilyak
LOCATION OF UV LAMPS RELATIVE TO THE FLOW

Lamps along the (air or water) stream. Longitudinal flow.

Lamps across the (air or water) stream. Cross-flow.

UV lams in quartz sleeves

Slide courtesy of L. Vasilyak
UFA city, Russia. 3 UV units UDV-216A.

UV units UDV-216A: Capacity 3600 m³/h. 216 UV lamps DB 300
WASTE WATER: MOSCOW WWTP.

ASIA AND EUROPE’S LARGEST UV SYSTEM.

3,125,000 m³/day (180,000 m³/hr)

17 channels,
170 UV units,
6,120 UV lamps DB600
UVc use for disinfection of air

- **The** Second Gilbert W. Beebe Webinar: Safety and Efficacy of UVC to Fight COVID-19
- Upper room germicidal irradiation was successfully used to prevent measles
- It was shown that germicidal UVc prevented TB infection of guinea pigs breathing infected air for 3 days. Guidelines for dosing M. Mphaphele … Ed Nardell Am J Respir Crit Care Med.

Guidelines are well developed to reduce scattering from ceiling.
Mean wavelength-dependent UV absorbance coefficients averaged over published measurements for eight common substances.
Far-UVC safety studies

60 Week Exposure Safety Study
100 SKH-1 hairless mice exposed
8 hrs / day to graded high doses
of 222-nm far-UVC light

50 weeks into the study:
No skin lesions, no eye issues
Far-UVC efficacy studies

Far-UVC inactivation of aerosolized coronaviruses

TCID$_{50}$ technique

Buonanno et al 2020
UVc 220 nm use for disinfection of air

- UVC 220 nm were shown to be safe on people skin and eyes can be used in rooms with people

Intranasal fusion inhibitory lipopeptide prevents direct contact SARS-CoV-2 transmission in ferrets.

- Rory D. de Vries. Intranasal fusion inhibitory lipopeptide prevents direct contact SARS-CoV-2 transmission in ferrets | bioRxiv

- Daily intranasal administration to ferrets completely prevented SARS-CoV-2 direct-contact transmission during 24-hour co-housing with infected animals, under stringent conditions that resulted in infection of 100% of untreated animals.
Use of various ointments to protect infection through nasal passages

• Oxolini unguentum (have been used in Russia against flue for decades)

• Plasma-activated water with nanoparticles (stomach infection, possibly effective for nasal wash)
Plasma treated water

Fig. 1. Assumption of chemical reactions in plasma treated liquids [54] ©2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.
Role of PH in water

PAWs killed bacteria through the same mechanism as plasma by inducing cell membrane damage.


Evidence

Peng Sun, et al.

b) untreated and c) treated with PAW-Air-30 for 3 h

TM13.00008: Osmotic pressure on cell or virus membranes in a saline interacting with weakly ionized plasma. Mikhail Shneider, Mikhail Pekker

Pulsed arc system for inflow production of plasma-activated water with silver nanoparticles for biological applications

Pavel Dourbal, Tatiana Aristova, Igor D. Kaganovitch

APS-DPP 2020 abstract Abstract: VM09.00005
Efficient in-water plasma generation on silver electrode

- Plasma is controlled with a magnetic amplifier
- Control loop feedback directly proportional to an impedance of the plasma: positive feedback by voltage, negative by current not clear
- Matches plasma power to water conductivity not clear
- Ignores and maintains plasma; No separate plasma igniter circuit is required
- US Patent 9,343,996
Healing psoriasis, eczema, dry skin

Topical application 2 times daily with coconut oil. These psoriatic skin lesions existed for over 45 years.

August 2018

November 2018, and counting
Two size populations of silver nanoparticles are present

Sample data:

<table>
<thead>
<tr>
<th>Diam. (nm)</th>
<th>% Volume</th>
<th>Width (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak 1:</td>
<td>42.05</td>
<td>40.0</td>
</tr>
<tr>
<td>Peak 2:</td>
<td>155.49</td>
<td>60.0</td>
</tr>
<tr>
<td>Peak 3:</td>
<td>0.00</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Polydispersity Index: 0.243

Summary results:

- 40% of 42.05nm
- 60% of 155.49nm

Average Size: 110.114nm

Surface Area: 0.108cm^2/mL
Questions?

Contact Inventor
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Conclusions

For indoor safety integrating approach estimating allowable infection dose should be studied taking into account ventilation, possible aerosol spread and active UV disinfection (254nm with safety glass and gloves, <222nm possibly safe as is!).

Use of nasal treatments/washes to prevent virus binding could be effective mean to prevent infection.

BACK UP SLIDES
**R₀** is the number of people a newly infected patient is expected to infect.

Herd immunity: when the fraction of people who have not had the disease is \(< 1/R₀\) (measles: \(R₀ = 16\); Covid19: \(R₀ = \sim 2.7\))
Speculative conclusions

- Breathing and speech particles are far more numerous than assumed
- Most speech droplets stay airborne for minutes, not hours
- Indoors: no safe physical distance
- Nose breathing 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!
Adriaan Bax
The airborne lifetime of small speech droplets and their potential importance to transmissibility of SARS-CoV-2

Valentyn Stadnytskyi, a Christina E. Bax, b Adriaan Bax**, and Philip Anfinrud**

PNAS May 13, 2020 117 11875-11877; doi.org/10.1073/pnas.2006874117

\[ I(t) = 7 \exp(-t/14 \text{ minutes}) \]

\[ I(t) = 2 \exp(-t/8 \text{ minutes}) \]

480-frame overlay (Yang Shen)

Illuminated window: 30 ml. Box volume: 200 L
Is there an infectious threshold for a susceptible host?

Many bacterial pathogens result in infection if the immune system gets overwhelmed (e.g. wounds; aspirational pneumonia; high local pathogen concentration)

Respiratory virus comes in units of 1, and “landing sites” are far apart

The probability of a virus entering a host cell and creating 1000 progeny is low (~ 0.01 – 1 %)

Exponential growth: $1 \times e^{t/4h}$ vs $10 \times e^{t/4h}$
DNA - A KEY TARGET MOLECULE FOR

IES Germicidal Action Spectrum
(after Gates and others)

...for bacteria and some viruses, but also the susceptible molecule in eye or skin!

Adenine
Guanine
Thymine
Cytosine

But SARS-CoV-2 is a RNA virus!
OCCUPATIONAL SAFETY ISSUES

• Ultraviolet Safety is a very important issue!

• Accidental exposure of skin & eyes:
  • Photokeratitis ("welder’s flash," or “snowblindness”) – with symptom of “sand in the eyes” - Cornea is most sensitive tissue
  • Erythema – reddening of the skin
    • Can be severe if penetrating UV-B rays ("sunburn")
    • Mild if UV-C – very superficial absorption

• Delayed Effects

• Skin Cancer?
  • UV-B in sunlight penetrates to basal (germinative) layer of epidermis and is the recognized cause of most skin cancers
  • UV-C heavily absorbed in superficial epidermis & stratum corneum
WHAT ARE THE SAFETY GUIDELINES FOR HUMAN EXPOSURE IN THE GUV UV – C BAND

• Action spectrum for safety is the ACGIH/ICNIRP/CIE/ISO/IEC action spectrum $S(\lambda)$

$$E_{\text{eff}} = \sum_{180}^{400} E_\lambda \cdot S(\lambda) \cdot \Delta \lambda$$

• $S(\lambda)$-spectral weighting leads to an effective radiant exposure of 3.0 mJ/cm² (30 J/m²)

• Limit is daily – including multiple exposures

• Time-weighted average (TWA) over a day

• At 254 nm this is 6 mJ/cm² (60 J/m²)
  • Or, time-averaged irradiance of 0.2 µW/cm²

• Large safety margin for human skin in UV-C – Should there be two limits? – For the Eye, For the Skin?

ACGIH UV $S(\lambda)$ spectral weighting function (action spectrum) is the solid line.

$S(\lambda) = 1.0$ at 270 nm

$S(\lambda) = 0.5$ at 254 nm
IS THERE A REALISTIC SKIN CANCER RISK?

THE FIRST LAW OF PHOTOBIOLOGY – PHOTONS HAVE TO BE ABSORBED TO PRODUCE AN EFFECT – AND THEY HAVE TO REACH THE TARGET MOLECULES

• TYPICAL CONCERN – If UV-C has highest photon energy why is it not more phototoxic and a more severe skin cancer risk??
  • UV-B photons are less energetic but they penetrate deeper
  • Bruls transmission measurements


Sunlight spectrum – only trace amounts of UV-B reach ground level and no UV-C at all (Sliney & Wolbarsht, 1980); Sliney DH, Balancing the Risk of Eye Irritation from UV-C with Infection from Bioaerosols†2013