RESPIRATORY PROTECTION: RECENT RESEARCH DEVELOPMENTS

ORGANIZATION FOR SAFETY, ASEPSIS AND PREVENTION SYMPOSIUM, ATLANTA, GA
JUNE 21-23, 2012

Raymond Roberge, MD, MPH
National Personal Protective Technology Laboratory, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention

ANTIMICROBIAL-TREATED FILTERING FACEPIECE RESPIRATORS

- POTENTIAL BENEFITS
  - greater protection from pathogens penetrating filter media
  - extended useful life of FFR
  - HCW use between different patients
  - no need for decontamination
  - elimination of fomite potential of FFR
  - elimination of re-aerosolization threat
  - greater shelf life

- POTENTIAL DOWNSIDES
  - higher cost
  - effects of additional layer (charcoal) required for one model
  - availability

FATE OF MICROORGANISMS TRAPPED BY RESPIRATORY PROTECTIVE FACEMASKS

- SURVIVAL
  1) Fomite

- GROWTH
  2) Reaerosolization

- DEATH
FOMITE

- MS-2 virus (5 drops of 5 µL each) loaded onto N95 filtering facepiece respirators and other personal protective equipment after donning
- Equipment doffed as per CDC protocol and virus sampling of hands undertaken.
- Transfer of virus to both hands identified in a majority of subjects

REEAEROSOLIZATION RESEARCH

- Quian Y et al: Aerosol Sci Technol 1997;27:394-404 - reentrainment of 0.6 – 5.1 µm particles from polypropylene filters increases with approximately the square of the particle size and the air velocity, and decreases with increased humidity and filter thickness (most re-entrained particles come from the outer surface)
- Birkner JS et al: J Occup Environ Hyg 2011;8:1-9 – dropping filtering facepiece respirators loaded with 20 million particles from 0.76 meter height results in 0.002% - 0.012% particle release
- Birkner JS et al: J Occup Environ Hyg 2011;8:10-12 – doffing filtering facepiece respirators loaded with 20 million particles results in release of a negligible number of particles
- Fisher et al: Am Occup Hyg 2012;56:315-325 – 1.3 x 10^4 and 1.3 x 10^5 MS-2 droplet nuclei loads on N95 filtering facepiece respirators produced only 0.21% and 0.08% reaerosolization rates following simulated coughing

RESEARCH ON THE FATE OF MICROORGANISMS ON PROTECTIVE FACEMASK

QUESTION 1 – DO MICROORGANISMS SURVIVE ON PROTECTIVE FACEMASKS?

- Multiple studies of filters and surfaces of filtering facepiece respirators and surgical masks that have been carried out with various microorganisms, indicate that microorganisms can survive on respiratory protective device surfaces and filters.

- Mycobacterium (tuberculosis, avium, etc.)
- Bacillus (subtilis var niger, atrophaeus)
- Staphylococcus epidermidis
- Pseudomonas flourescens
- MS-2 phage
- H1N1
- H3N2
- avian influenza virus
- human adenovirus serotype 1

- Survival time is variable (hours to weeks) based upon:
  - The microorganism involved (e.g., spores are harder than bacteria)
  - Microorganism features (e.g., enveloped viruses are more susceptible to environmental stressors than non-enveloped viruses)
  - Protection factors (in respiratory secretions)
  - Availability of nutrients

QUESTION 2 – DO MICROORGANISMS MULTIPLY ON PROTECTIVE FACEMASKS?

Numerous studies indicate that microorganisms do not multiply on respiratory protective equipment. Reasons for lack of reproduction include:

- Insufficient nutrition - (microorganisms generally cannot utilize polypropylene for nutrition)
- Hydrophobicity of polypropylene
- Porosity – the majority of viruses remain viable longer on nonporous surfaces than porous surfaces

ANTIMICROBIAL-TREATED RESPIRATOR RESEARCH AT NPPTL

- Viruses consist of two or three parts: all viruses have genes made from either DNA or RNA, all have a protein capsid; and some have a lipid envelope that surrounds them when they are outside a cell.
- Viruses are nonliving infectious agents.
- Viruses with an envelope (influenza) are easier to inactivate.

<table>
<thead>
<tr>
<th>FR</th>
<th>Active Component</th>
<th>Mode of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR A</td>
<td>Silver</td>
<td>Deactivates the virus's metabolism, preventing reproduction</td>
</tr>
<tr>
<td>FFR B</td>
<td>Iodine</td>
<td>Attacks key groups of proteins, nucleotides, and fatty acids, leading to cell death</td>
</tr>
<tr>
<td>FFR C</td>
<td>Ozone-like</td>
<td>Attacks the protein capsid, liberates the nucleic acid, and inactivates the nucleic acid</td>
</tr>
<tr>
<td>FFR D</td>
<td>Quaternary Ammonium Compound (QAC)</td>
<td>Attacks the cytoplasmic (inner) membrane in bacteria or the plasma membrane in yeasts</td>
</tr>
<tr>
<td>FFR E</td>
<td>Titanium Dioxide and UV</td>
<td>Oxidizes membrane or cell wall, deactivates the virus's metabolism, and prevents reproduction</td>
</tr>
</tbody>
</table>

ANTIMICROBIAL-TREATED RESPIRATOR TEST METHOD MATERIALS

- Aerosol medium - 1% growth medium containing: tryptone, yeast extract, sodium chloride, glucose, magnesium chloride, and thiamine.
  - Provides protection to the virus.
  - Chemical.
  - Physical.
- MS2.
  - Bacteriophage specific to Escherichia coli.
  - BSL-1.
  - Used as a surrogate for pathogenic viruses.
  - RNA as genetic material.
  - Non-enveloped.

ANTIMICROBIAL-TREATED FILTER TEST METHOD RATIONALE

- Filtering facepiece respirator coupons were stored at 22°C and 30% relative humidity for 8 and 20 hours.
  - The environmental conditions were chosen to represent likely environmental conditions of a hospital.
  - Storage time of 8 hours was chosen to represent a normal work shift.
  - 20 hour time point added after initial tests.

ANTIMICROBIAL-TREATED FILTER TEST METHOD

- $10^6$ MS2 applied to coupons.
- Store at 22°C and 30% RH 8 and 20 hours.
- Recover and quantify virus.
- Calculate log reduction for storage control and antimicrobial.

Log reduction = $\log_{10}(LL/Storage Control)$

Log reduction = $\log_{10}(LL/Antimicrobial)$

$\times 3$
MS2 SURVIVAL ON FFR COUPONS
Stored at 22°C and 30% relative humidity

- MS2 can serve as the test virus
- FFRs may harbor infectious virus (fomite)

SECOND SET OF TEST CONDITIONS
- The coupons were stored at 37°C and 80% relative humidity for 2 and 4 hours
  - The environmental conditions were chosen to loosely represent the microenvironment of an FFR while in use
  - Storage time of 2 and 4 hours was chosen to represent the time of FFR use
- The FFR containing Titanium Dioxide/UV was not included in this study

RESULTS
Storage at 22°C and 30% RH

- 8 Hour Time Point
- 20 Hour Time Point
RESULTS

22°C and 30% RH  37°C and 80% RH

INTERPRETING THE RESULTS

- Two of the FFRs contained AT that targeted microbial components inconsistent with the test virus
- None of the FFRs with AT demonstrated virucidal activity at 22°C and 30%RH
- The FFR using EnvizO3-Shield™ technology did not show decontamination efficacy under any condition despite a promising mode of action
  - Is it the effect of the formation of a droplet nuclei?
- The FFR containing iodine technology proved to be effective at higher temperature and relative humidity

IODINE-BASED ANTIMICROBIAL RESPIRATORS

   - Comparison of two N95 filtering facepiece respirators, with an iodinated P95 FFR, challenged with aerosolized MS-2 @ 85 LPM
   - No significant difference in viable virus penetration of the control and iodinated respirators
   - Particle penetration was significantly less for the iodinated FFR (hypothesized to be due to the physical properties of the iodine resin and an enhancement of electrostatic properties)
   - Comparison of iodine-based N95 filtering facepiece respirators (MS-2 virus) and similar untreated FFRs challenged with MS2 virus, Staphylococcus aureus and B. atrophaeus spores @ 85 LPM
   - No significant difference in viable particle penetration of MS2 plaque
   - Aerosol loading of H1N1 and H5N1 influenza indicated no difference in viable particle penetration between standard N95 FFRs and iodine-based antimicrobial N95 FFRs
   - Comparison of iodine-based and citric acid-based N95 FFR models with controls @ 85 LPM after challenge with aerosolized H1N1 influenza
   - No significant difference between controls and antimicrobial N95 FFR with respect to penetration of viable H1N1 influenza virus
METAL IMPREGNATED FIBERS AND FABRICS (COPPER OXIDE; SILVER)

   • 2.2% copper oxide impregnated N95 filtering facepiece respirator vs similar untreated controls @ 28.3 LPM
   • copper did not impair filtration (similar numbers of infectious influenza A and avian influenza viral titers passed through the test and control respirators)
   • significantly greater levels of infectious virus titers on untreated respirators 30 min after challenge
   • authors state “no significant additional cost” to produce copper oxide respirators

   • 10 µL of either of two strains of H1N1 applied to 2 cm² pieces of silver-impregnated non-absorbent polyester fabric (hospital gown material)
   • Surface sampling at 1 minute and 4, 9, 24, 48, and 72 hours.
   • Viable virus recovered at 4 hours

CONCLUSIONS

• The decontamination efficacy of antimicrobial respirators is likely to be different for enveloped viruses such as influenza

• Influenza virus viability on antimicrobial respirators cannot be estimated from the MS2
  – Co-contamination of FFRs with influenza and other more resilient infectious microbes
  – Emergence of unknown microbial threats

• Virus contamination method (droplet nuclei, droplet) may affect decontamination efficacy

• Antimicrobial FFRs may not be designed for surface inactivation

DECONTAMINATION OF FILTERING FACEPIECE RESPIRATORS

[Image of decontamination process]
Background – 2006 IOM Report

- Over 90 million N95 FFRs for healthcare workers during a 42-day outbreak
- Can disposable FFRs be reused?
  - (1) remove the viral threat, (2) be harmless to the user, and (3) not compromise the integrity of the FFR
- Minimal data exists
- Current test methods are not practical

CHEMICAL DECONTAMINATION METHODS

- Ethylene oxide (EtO) – 55°C and 725 mg/L\(^{-1}\) 100% EtO gas x 1 h followed by 4 h aeration
- Vaporized hydrogen peroxide (VHP) x 55 min
- Bleach – 30 min submersion in 0.5% bleach in tap water and overnight air drying
- Soap and H\(_2\)O – 1 gram of detergent in 1 liter of tap water soaked x 2 min
- Isopropanol (70%) – dunked x 1 second

PHYSICAL DECONTAMINATION METHODS

- 1100 Watt Microwave (2450 MHz) – power setting of 10 (maximum) with revolving plate exposure x 1 min for each side
- Ultraviolet Germicidal Irradiation (UVGI) – (40 watt lamp, 254 nm) x 15 min each side (176-181 mJ/cm\(^2\) exposure)
- Dry Heat – 160 – 180°C oven x 60 min
- Autoclave – 121°C at 15 psi x 30 min
**DECONTAMINATION TECHNIQUES**

<table>
<thead>
<tr>
<th>Decon Method</th>
<th>Recommended Concentration or Level</th>
<th>Recommended Effective Contact Time</th>
<th>Effective Level &quot;Less&quot;</th>
<th>Effective Level &quot;More&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>EtO</td>
<td>500 – 1000 mg/L 58%</td>
<td>1-12 hours 45 minutes 10 – 30 minutes</td>
<td>3M XDL 75 mL</td>
<td>3M XDL 803 mL</td>
</tr>
<tr>
<td>Bleach</td>
<td>0.5% in tap H2O 6%</td>
<td>10 minutes 2 minutes 10 – 30 minutes</td>
<td>DERMAD NT</td>
<td>DERMAD 100S</td>
</tr>
<tr>
<td>H2O2</td>
<td>1 gram/L 75%</td>
<td>2 minutes 3 minutes dunk 1 second</td>
<td>dunk 5 minutes</td>
<td>dunk 6%</td>
</tr>
<tr>
<td>Soap &amp; H2O</td>
<td></td>
<td>10 – 30 minutes</td>
<td>20 minutes dunk 1 minute</td>
<td></td>
</tr>
</tbody>
</table>

| Microwave    | full power 10WV                  | 2 minutes 60 minutes 30 minutes | 4 minutes            | 30 minutes             |
| UVGI         | 254 nm full distribution         | 2 minutes 60 minutes 30 minutes | 4 minutes            | 30 minutes             |
| Heat         | 105 – 106 °C                     | 2 minutes 60 minutes 30 minutes | 4 minutes            | 30 minutes             |
| Autoclave    | 121 °C @ 15 psi                  | 2 minutes 60 minutes 30 minutes | 4 minutes            | 30 minutes             |

**EFFECT OF DECON ON FILTRATION & APPEARANCE (PHASE 1)**

- **Experimental Design**
  - 1 N95 FFR, 1 P100 FFR
  - Automated systems: autoclave, VHP, EtO
  - Chemical: IPA, Bleach, LHP, Soap & Water
  - Physical: UV, microwave, heat
  - Controls: water, no decon

**RESULTS (PHASE 1)**

- Autoclave: significant filter or physical degradation
- 160° C dry heat: degraded filter performance, but particle penetration levels were still w/i expected levels
- EtO: caused no significant change in filter performance
- Bleach: degradation
- Soap & water: degradation
- UVGI: degradation
EFFECT OF DECON ON FILTRATION % APPEARANCE (PHASE 2)

- Experimental Design
  - 9 FFR models: 3 N95, 3 Surgical N95, 3 P100
  - “Low temperature” (<90°C) decontamination methods
  - Bleach, UV, VHP, EtO, and Microwave

RESULTS (Phase 2)

- Effects were model specific. FFRs tested have difference in their design (e.g., # of layers, face seal enhancements) and materials of construction (e.g., hydrophobicity)
- Inner face seal liner (P100) and material near metal nose clip (Surgical N95) on two FFR model melted in microwave
- All other combination had expected levels of laboratory performance (filtration efficiency, air flow resistance)
- Bleach had noticeable odor – even after drying 22 hours – and low levels of chlorine gas were found after rehydration

UVC Treatment of FFRs

Two sided treatments

- 10 min.
- 5 min.
- 5 min.
THE WHO & WHY OF UVGI

- **Who?**
  - Manufacturers and policy makers for the purpose of FFR design and pandemic preparedness planning

- **Why?**
  - Technology is readily available
  - Easy and inexpensive method
  - Physical methods are less likely to leave hazardous residues
  - Research has demonstrated no adverse effects of UVGI on filtration and fit for the tested FFR models

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CRITICAL QUESTIONS

- Can UVGI penetrate into the multiple layers of the FFR?

- Can UVGI inactivate virus deposited as droplet nuclei on and within the multiple layers of an FFR?

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FFR LAYERS

- **Exterior layers**
  - Have multiple functions
    - Comfort
    - Form and fit
    - Strength and protection

- **Filtering Layer(s)**
  - Electret filtering medium
    - Similar across models
    - Very distinctive visually
    - Provides the majority of the filtration for the FFR
    - Multiple layers
**UVGI TEST VIRUS AND FFRs**

- **MS2**
  - Smaller genome has fewer potential targets

<table>
<thead>
<tr>
<th></th>
<th>MS2</th>
<th>Influenza A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Envelope</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Genome</td>
<td>ssRNA (3.5 kb)</td>
<td>ssRNA (13.6 kb)</td>
</tr>
</tbody>
</table>

- **Six FFRs**
  - 3 surgical N95 FFRs
  - 3 particulate N95 FFRs

**UVGI TREATMENT OF FFRs: TRANSMISSION AND DECONTAMINATION EFFICACY**

- Transmittance of UVGI through layers of FFRs (2 directions)

- Decontamination of MS2 contaminated coupons

<table>
<thead>
<tr>
<th></th>
<th>5 min.</th>
<th>5 min.</th>
<th>10 min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity</td>
<td>2500 µW/cm²</td>
<td>UV-C</td>
<td></td>
</tr>
<tr>
<td>#1</td>
<td>2020</td>
<td>690</td>
<td>461</td>
</tr>
<tr>
<td>#2</td>
<td>230</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>#3</td>
<td>2533</td>
<td>36</td>
<td>1</td>
</tr>
</tbody>
</table>

**UVCT THROUGH FFR COUPONS**

- Calculation of UVGI (%) interacting with the IFM

<table>
<thead>
<tr>
<th></th>
<th>3M 1860</th>
<th>2500</th>
<th>2020</th>
<th>690</th>
<th>461</th>
<th>37</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFM 1</td>
<td>2533</td>
<td>0</td>
<td>1810/5000</td>
<td>50.6%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFM 2</td>
<td>230</td>
<td>2500</td>
<td>0</td>
<td>0</td>
<td>2.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFM 3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>426/5000</td>
<td>8.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFM 4</td>
<td>1</td>
<td>426</td>
<td>0</td>
<td>0</td>
<td>8.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFM 5</td>
<td>1</td>
<td>2533</td>
<td>0</td>
<td>0</td>
<td>50.6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Intensity = µW/cm²
TRANSMISSION THROUGH FFR COUPONS

• UVC transmission through layers of Surgical N95 FFRs

### AVAILABLE UVGI

• Available UVGI for layers of Particulate and Surgical N95 FFRs (2 sided measurement)

• FFRs categorized by available UVGI for filtering layers

### UVC TREATMENT OF FFRs: LIGHT ABSORPTION

• Absorption of UVC by layers of Particulate and Surgical N95 FFRs (2 sided measurement)

• FFRs categorized by absorption of filtering layers
CONCLUSIONS (UVGI)

• UVGI can penetrate to the internal filtering layers of FFR but is model specific
• UVGI inactivates MS2
• FFRs demonstrating limited UVGI transmission may also be decontaminated with an increase in treatment time or UV irradiance
• The effect of the 3D shape of the FFR may affect decontamination efficiency

FINAL CONCLUSIONS

• There are no approved methods for the decontamination of disposable N95 FFRs
• FFRs may serve as fomites
• Current antimicrobial respirator testing may not accurately characterize “real world” scenarios (i.e. droplet nuclei vs. droplet)
• UVC decontamination is promising
  – Inactivates virus
  – Not harmful for the wearer
  – Does not impact the integrity of the tested FFRs

Publications

- Fischer, E., and Shaffer, R.E., A Method to Determine the Available UVC Dose for the Decontamin...
PUBLICATIONS


Fisher E, Shaffer R. Survival of Bacteriophage MS2 on Filtering Facepiece Respirator Coupons. Applied Biosafety. Accepted 2010

Fisher E, Shaffer R. A Method to Determine the Available UV-C Dose for the Decontamination of Filtering Facepiece Respirators. 2010. Submitted to Journal


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