Pulmonary and Systemic Immune Response to Inhaled Oil Condensates

Jake McDonald
Loveland Respiratory Research Institute
Nanoparticles are a Topic of Interest

- Interest driven by a few studies, mostly with non-environmental particles
- Consideration of particle number standards
- Particle mass going down (thanks to you)
- Not certain if nanocondensates will be removed as quickly as solid “soot”
  - Limited information on hazard of this material
Solid and liquid particles may “behave” differently at lung surface.

ULTRAFINES/NANOPARTICLES
Aerosol Exposures

- Mice exposed by nose-only inhalation 6 hr/day for 7 days (*match diesel protocols*)
- Shell Rotella-T15w-40 oil from 200 hr change in Cummins 5.9L engine on FTP cycle
- Oil nanocondensates generated by evaporation/condensation
- Diluted to target of $10^6$ particles/cm$^3$ at a <20 nm particle size
Exposure Atmosphere

- Median diameter: 17 nm
- Particle Mass: 300 µg/m³
- Particle Count: 10⁶ p/cc
- Surface Area: 25 nm²/cc
- Vapor HC: 0.6 ppm
- CO: 0.3 ppm
- NOx: < 40 ppb
- Additional analyses underway

Calculated dose, assuming 50% deposition, = 2 µg/day
Measurements of Response

Mice exposed to clean air or oil

- Change in inflammatory cells in lung
- Change in biochemical indicators of injury, inflammation or chemical stress in lung or serum
- Presence of particles or lung tissue damage assessed by light microscopy
- Change in systemic immune response
Does exposure increase response to a known irritant?

- Separate group of mice exposed (on day 4) by inhalation to ~5 µg inhaled dose of bacterial cell walls to induce inflammation
  - Similar to “bronchitis”
- Measured same endpoints as non-LPS
No increase in inflammatory cells

**Lavage Cells**

**Total Cells**

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>OIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells/ml x 10^6</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**Macrophages**

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>OIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells/ml x 10^6</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**Neutrophils**

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>OIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells/ml x 10^3</td>
<td>1.25</td>
<td>1.25</td>
</tr>
</tbody>
</table>

**Lymphocytes**

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>OIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells/ml x 10^3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
Most Biochemical Indicators Did Not Increase with Exposure

Also did not see increase in inflammatory cytokines
A Sensitive Indicator of Oxidant Stress \textit{DID} Increase

Heme Oxygenase-1 Protein

Relative Band Intensity

- FA
- OIL
LPS induced injury/inflammation not exacerbated by nanocondensates

**Inflammatory Histopathology**

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Sum of Inflammation/mouse mean and SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>1.5</td>
</tr>
<tr>
<td>LPS</td>
<td>3.2</td>
</tr>
<tr>
<td>Oil</td>
<td>1.1</td>
</tr>
<tr>
<td>LPS/OIL</td>
<td>4.0</td>
</tr>
</tbody>
</table>

LPS/OIL significantly greater than from FA/OIL
Immune Response Decreased After Nanocondensate Exposure

* statistically significant difference with air control (P < 0.05)

n=7 mice/group
Summary and Future Directions

• Inhaled nanocondensates showed very limited response for pathology, inflammatory cells, and biochemical indicators.

• While oil may have driven response to instilled material in previous studies with rats, it appears to be only mildly toxic at lower and inhaled doses in mice

• Only most sensitive indicators (oxidant stress/systemic immunity) showed physiological response to inhaled nanocondensates

  — These results to be confirmed and extended to no-effects levels
  — Results to also be compared with new oil, oil obtained from gasoline engines and nanosulfate for comparison.

IS NANOTOX = NANOHYPE??
Acknowledgements

• Funding Provided by Health Impacts Program of DOE-FCVT.
  – Dr. James Eberhardt, Project Manager

• Contributors
  – Joe Mauderly
  – JeanClare Seagrave
  – Andrew Giggliotti
  – Scott Burchiel (UNM)
  – Leah Mitchell
  – Ramesh Chand