US EPA ARCHIVE DOCUMENT
Exhaled nitric oxide in children with asthma:
1) Outdoor- versus indoor-generated PM
2) Short term PM exposure

Therese Mar, Ryan Allen, Karen Jansen, Jane Koenig, Timothy Larson, Thomas Lumley, Sally Liu
University of Washington
Background

- Exhaled nitric oxide (eNO) is a ubiquitous molecule in the body and is a non-invasive marker of airway inflammation
- eNO is known to be elevated in individuals with asthma, is increased when a subject is having an asthma attack, and is decreased in those individuals using corticosteroid medication
- eNO has been compared with other techniques for measuring inflammation (ex. breath condensate, induced sputum)
Subject Characteristics

- 19 subjects: 14 male, 5 female
- Ages 6-13
- Medication use:
  - 10 inhaled corticosteroid (ICS) users
  - 9 ICS nonusers
- FEV1%: 67-100%
Data Collection

\( \text{PM}_{2.5} \)

- Local outdoor (HI)
- Local indoor (HI)
- Personal (HPEM)
- Average of 3 central sites: Kent, Lynnwood, and Lake Forest Park (TEOM)

Health Endpoint

- Daily concentration of eNO (ppb)
Estimating Exposure to Ambient and Non-ambient PM
Source-Specific Exposure Model

\[ E_t = E_a + E_{ig} + \text{“personal cloud”} \]

\[ E_a = [y + (1-y)(F_{inf})]C_a \]

\[ E_{ig} = (1-y)(C_{ig}) \]

\[ \alpha = \text{“attenuation factor”} \]

\[ E_t = \text{HPEM or pDR} \]

\[ y = \text{fraction of time spent outdoors} \]
\[ C_a = \text{ambient (outdoor) concentration (HI or neph)} \]
\[ C_{ig} = \text{indoor-generated concentration} = C_i - C_a(F_{inf}) \]
\[ C_i = \text{indoor concentration (HI or neph)} \]
Results

• Associations between various measured PM metrics and exhaled NO
• Associations between estimated concentrations of outdoor- and indoor-generated PM2.5 and eNO
Results ICS nonusers
eNO, ppb (95% CI)

For a 10 ug/m$^3$ increase in PM$_{2.5}$, eNO increase

• Personal: 4.5 (1.02, 7.9)
• Indoor: 4.2 (1.02, 7.4)
• Outdoor: 4.3 (1.4, 7.2)
• Central: 4.2 (1.2, 6.4)
• EIG: -3.3 (-1.1, 7.7)
• EAG: 5.0 (0.3, 9.7)

– No effects were seen in ICS users
Previous findings

- Exhaled NO is a feasible, non-invasive technique for measuring airway inflammation
- Various measures of PM$_{2.5}$ were associated with a marker of airway inflammation in children with asthma
- Inhaled corticosteroid use attenuated the association between eNO and PM$_{2.5}$
- Other panel studies have reported associations between PM$_{2.5}$ and eNO. (Adamkiewicz et al, 2004; Jansen et al, 2004)
Short term analysis

• Objectives:
• To determine the effect of short term PM exposure (hourly lags) on exhaled nitric oxide
Methods

• Polynomial distributed lag model
• Hourly lags of PM up to 48 hours
• Model controlled for temperature, relative humidity, ambient NO concentrations and medication use
Polynomial distributed lag model

\[ E[Y] = B_0 + b_i + B_1(Z_{1\text{ids}} - \overline{Z}_{1\text{is}}) + B_2\text{med}_i + B_3\text{med}_i \ast (Z_{1\text{ids}} - \overline{Z}_{1\text{is}}) \]

\[ + B_4(Z_{2\text{ids}} - \overline{Z}_{2\text{is}}) + B_5\text{med}_i \ast (Z_{2\text{ids}} - \overline{Z}_{2\text{is}}) + B_6(Z_{3\text{ids}} - \overline{Z}_{3\text{is}}) \]

\[ + B_7\text{med}_i \ast (Z_{3\text{ids}} - \overline{Z}_{3\text{is}}) + B_8(Z_{4\text{ids}} - \overline{Z}_{4\text{is}}) + B_9\text{med}_i \ast (Z_{4\text{ids}} - \overline{Z}_{4\text{is}}) \]

\[ + B_{10}(W_{\text{ids}} - \overline{W}_{\text{is}}) + B_{11}\text{age} + B_{12}\text{rh} + B_{13}\text{temp} \]

where

\[ Z_1 = \sum_{n=1}^{24} P\text{Mlag}_n, \quad Z_2 = \sum_{n=1}^{24} n \ast P\text{Mlag}_n, \quad Z_3 = \sum_{n=1}^{24} n^2 \ast P\text{Mlag}_n \quad \text{and} \quad Z_4 = \sum_{n=1}^{24} n^3 \ast P\text{Mlag}_n \]

W is the ambient NO concentration
## Averaged PM effect

<table>
<thead>
<tr>
<th>PM</th>
<th>change in eNO per 10 µg/m³ PM</th>
<th>95% Lower CI</th>
<th>95% Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>lag 1 hour</td>
<td>7.16</td>
<td>3.72</td>
<td>10.59</td>
</tr>
<tr>
<td>lag 4 hour</td>
<td>6.39</td>
<td>2.85</td>
<td>9.93</td>
</tr>
<tr>
<td>lag 8 hour</td>
<td>0.56</td>
<td>-1.07</td>
<td>2.20</td>
</tr>
<tr>
<td>PM 2.5 averaged from 7pm to 4 am</td>
<td>1.61</td>
<td>0.15</td>
<td>3.07</td>
</tr>
<tr>
<td>PM 10 averaged from 7 pm to 4 am</td>
<td>2.27</td>
<td>0.78</td>
<td>3.77</td>
</tr>
</tbody>
</table>
effect of lags on eNO

change in eNO (ppm)

lag (hr)
Conclusions

• eNO is associated with PM exposure up to 11 hours prior to eNO measurement
• An association between eNO and PM averaged during high wood smoke hours (7 pm to 4 am) was observed