AB 617 Biomonitoring Update: Biomarker Research and Potential Study Designs

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Office of Environmental Health Hazard Assessment
Presentation to Scientific Guidance Panel Meeting
November 12, 2020
The California Air Resources Board (CARB) established the Community Air Protection Program in response to AB 617, which aims to reduce exposures in communities disproportionately impacted by air pollution.

In collaboration with the University of California (UC), OEHHA is designing targeted biomonitoring studies in selected AB 617 communities to:

- Complement and validate ongoing air monitoring
- Increase understanding of exposures and potential health risks faced by residents
- Evaluate specific emission/exposure reduction measures
Exposure concerns and reduction strategies

- Air pollutants of concern include:
  - Criteria air pollutants, such as PM$_{2.5}$, NO$_x$
  - Polycyclic aromatic hydrocarbons (PAHs)
  - Volatile organic compounds (VOCs)
  - Metals and pesticides

- Community Emissions Reduction Plan (CERP) strategies include:
  - Emission reductions in ports, railyards, and refineries
  - Truck rerouting and prevention of truck idling
  - Vegetation planting
  - Street sweeping
  - Installation of air filtration in facilities like schools and senior centers, as well as in homes
AB 617 community air monitoring

- Aims to characterize local sources
- Will help inform the selection of study area for biomonitoring
- Provides hyperlocal air pollutant measurements to pair with biomonitoring results

San Joaquin Valley Air Pollution Control District (2019)
Practical considerations

- **Limited resources**
  - Current contract with UC sufficient to conduct one targeted biomonitoring study
  - Some contract funds can be re-directed to UC labs for biomarker analyses

- **COVID-19 emergency**
  - Affects potential study design
  - Could impact recruitment

→ Focus on urinary biomarkers only
Options for urinary biomarkers of exposure

- Hydroxy metabolites of PAHs, including:
  - Naphthalene (NAP)
  - Fluorene (FLU)
  - Phenanthrene (PHE)
  - Pyrene (PYR)

- Stable metabolites of VOCs, such as:
  - Acrolein
  - Acrylonitrile
  - Benzene
  - 1,3-Butadiene
  - Ethylbenzene
  - Xylene
Options for urinary measures of effect

- Markers of oxidative stress, including:
  - Malondialdehyde (MDA)
  - 8-Isoprostane
  - 8-Hydroxy-2’-deoxyguanosine (8-OHdG), 8-Oxo-2’-deoxyguanosine (8-oxodG)

- Urinary mutagenicity assays
Challenges with air pollution biomonitoring

- Interpretation of PAH and VOC biomarkers
  - Multiple sources of exposures
  - Short biological half-lives of metabolites (hours to days)
- Spatial and temporal variation in air pollution
  - Affected by season and meteorology
  - Regional air monitoring may not capture hyperlocal exposures

Photo credit: pxfuel.com
Viability of urinary PAH and VOC biomarkers

Selected PAH and VOC biomonitoring studies have shown:

- Correlations with air pollutants
- Differences in exposure profiles between communities
- Correlations with biomarkers of effect
- Links to changes in air pollution exposures

Photo credit: pxfuel.com
Urinary PAH metabolites before and after travel from Los Angeles to Beijing

- PAH metabolite levels significantly higher while in Beijing
- Daily PM$_{2.5}$: LA=14.6 µg/m$^3$, Beijing=67.6 µg/m$^3$
- Smoking: all non-smokers, adjusted for cotinine
- Diet: 8 hour fast prior to urine collection

Adapted from Figure 2, Lin et al. (2019)
Measurements of urinary 1-OHP, 8-oxodG and mutagenic activity among 72 urban Italian traffic policemen

Fig. 1 Plot of 1-OHP, mutagens and oxidative DNA lesions in traffic policemen. S1 collected after 2 days off from work; S2 collected after 6 consecutive workdays.

- Significant pre/post shift differences in biomarkers of exposure and effect
- Urinary mutagenic activity and 8-oxodG were significantly correlated with 1-OHP
- Prescribed low-PAH diet for 2 weeks prior; all non-smokers

Ledda et al. (2018)
### Urinary PAH and VOC metabolites before and after cook stove intervention

<table>
<thead>
<tr>
<th>Parent compound</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAP</td>
<td>- 38%*</td>
</tr>
<tr>
<td>FLU</td>
<td>- 31%*</td>
</tr>
<tr>
<td>PHE</td>
<td>- 21%</td>
</tr>
<tr>
<td>PYR</td>
<td>- 14%</td>
</tr>
<tr>
<td>Benzene</td>
<td>- 40%*</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>- 12%</td>
</tr>
<tr>
<td>Acrylonitrile</td>
<td>- 38%*</td>
</tr>
</tbody>
</table>

* p< 0.05

- **Intervention resulted in:**
  - Significant 56% decline in **PM$_{2.5}$** (measured by personal air monitoring)
  - Significant declines in urinary metabolites of NAP, FLU, benzene, and acrylonitrile

- **PM$_{2.5}$** significantly correlated with all PAH metabolites and some VOC metabolites

Adapted from Table 3 of Weinstein et al. (2020)
Urinary PAH metabolites correlated with PAHs in air

<table>
<thead>
<tr>
<th>Parent PAH in air</th>
<th>Urinary metabolite</th>
<th>Low PAH diet $\rho^*$</th>
<th>High PAH diet $\rho^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAP</td>
<td>$\sum\text{OH-NAP}$</td>
<td>0.87</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>1-OH-NAP</td>
<td>0.89</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>2-OH-NAP</td>
<td>0.42</td>
<td>0.20</td>
</tr>
<tr>
<td>FLU</td>
<td>$\sum\text{OH-FLU}$</td>
<td>0.55</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>9-FLU</td>
<td>0.22</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>3-FLU</td>
<td>0.67</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>2-FLU</td>
<td>0.68</td>
<td>0.54</td>
</tr>
<tr>
<td>PHE</td>
<td>$\sum\text{PHE}$</td>
<td>-0.09</td>
<td>0.13</td>
</tr>
<tr>
<td>PYR</td>
<td>1-OH-PYR</td>
<td>0.38</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* $\rho$=Pearson correlation coefficient; bolded numbers statistically significant ($p<0.05$)

- N=8 non-smoking CDC employees
- PAHs in air measured via personal monitoring
  - Medians ranged from 0.4 ng/m$^3$ for PYR to 921 ng/m$^3$ for NAP
- Selected metabolites of NAP and FLU strongly correlated with modeled air exposures

Adapted from Table 5, Li et al. (2010)
Important elements for air pollution biomonitoring

- Designing a well-controlled intervention that produces a sufficiently large change in exposure (~50%)
- Accounting for smoking and dietary exposures
- Measuring multiple biomarkers of exposure and effect
- Collecting spatially and temporally appropriate measures of air pollution
Potential Biomonitoring Study Designs
Multi-pronged approach

**Intervention**
- Air filtration in an elder care facility and/or school

**Biomonitoring**
- Samples collected pre- and post-intervention
- Biomarkers of exposure: PAH and VOC metabolites
- Biomarkers of effect (e.g., oxidative stress, mutagenicity)
- Smoking exposure biomarkers
- Specific gravity, creatinine

**Air monitoring**
- Indoor and outdoor air measurements of PAHs, VOCs, and other pollutants

**Study tools**
- Questionnaire on diet, smoking, and other potential sources
- Activity diary
Effectiveness of indoor air filtration

- Most air filtration systems filter out particulate matter only; others also capture VOCs
- Air filtration can reduce particulate matter 50-90%, depending on the system (Polidori et al. 2013, Bennett et al. 2018, San Francisco Department of Public Health et al. 2018)
- Previous studies suggest urinary PAH biomarkers can detect changes in PM$_{2.5}$ exposures as small as 50% (Weinstein et al. 2020)
Proposed intervention study design

**Study population**
Non-smoking residents and staff of elder care facility

Advantages of residents
- Assess exposures before and after installation of air filtration
- Control for diet and indoor vs outdoor activity

Advantages of staff
- Assess “cross-shift” changes in exposures (pre-shift + post-shift)
- Expanded demographics
Other design elements

- Indoor and outdoor air monitoring
  - Both gas-phase and particle-bound air pollutants
  - Compare to hyperlocal community monitoring levels
- Ultrafine particle analysis to examine likely sources

Wagner and Leith, 2001
Other approaches for consideration

- Non-targeted screening
  - New analytical methods that can more broadly screen for VOCs in ambient air
- Unmetabolized parent PAHs
  - Higher detection frequencies - capture additional PAHs
- Diagnostic ratios for PAHs

<table>
<thead>
<tr>
<th>Diagnostic ratio</th>
<th>Value</th>
<th>Source</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLU/(FLU+PYR)</td>
<td>&gt; 0.5</td>
<td>Diesel</td>
<td>Ravindra et al. 2008</td>
</tr>
<tr>
<td></td>
<td>&lt; 0.5</td>
<td>Gasoline</td>
<td></td>
</tr>
<tr>
<td>$\sum\text{PAH}<em>{\text{LMW}} / $\sum\text{PAH}</em>{\text{HMW}}</td>
<td>&gt; 1.0</td>
<td>Petrogenic</td>
<td>Oliveira et al. 2017</td>
</tr>
<tr>
<td></td>
<td>&lt; 1.0</td>
<td>Pyrogenic</td>
<td></td>
</tr>
</tbody>
</table>
Keys to success for air filtration intervention study design

- Design intervention that will result in sufficiently large reduction in particles and VOCs ($\geq 50\%$) and that is appropriate for short half-life exposure biomarkers.
- Pair indoor and outdoor air pollution measurements with multiple biomarkers of exposure and effect.
- Conduct study at a time and place with high ambient air pollution (e.g., winter months).
- Control for and/or assess the influence of other exposure sources (e.g., smoking, diet).
Other collaborative opportunities

Collect and biobank urine samples as part of existing longitudinal or cross-sectional studies to:

- Compare exposures over time (e.g., before and after emission reduction strategies are implemented)
- Compare exposures within communities (e.g., examine impact of proximity to local emission sources)
- Compare exposures between AB 617 communities and with other communities
- Examine relationship between air pollution exposures and health effects (e.g., asthma, lung inflammation)
Next steps

- Identify potential facilities for intervention study
- Continue research on biomarkers of exposure and effect
- Develop specific study strategies with collaborators at UC and CDPH
  - Secure additional funding for enhanced air monitoring and VOC filtration
- Ongoing engagement with communities and CARB
- Continue conversations about other collaborative opportunities
Collaborating institutions
Questions and Discussion
References cited


References cited (cont.)


