A Natural Experiment to Assess Prenatal Exposure to Air Pollution and Long-Term Health and Reproductive Outcomes

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During its operation, the mill was the largest single source of particulate pollution in Utah Valley.

Acute elevations in PM$_{10}$ levels during the winter months of inversions.

Mill closed from 1986-1987, resulting in a natural experiment to study the health effects of air pollution exposure.

**Mill operation associated with:**

- Increased respiratory hospital admissions
- Increased school absenteeism
- Increased cardiovascular and respiratory mortality


FIGURE 2—Monthly Mean and 24-Hour High PM$_{10}$ (fine particulate pollution) Levels, Utah Valley, April 1985–January 1988

Geneva Steel and Preterm Birth

Mill operation was also associated with increased preterm births.

Long-term effects of prenatal exposure to air pollution?

Prenatal exposures cause epigenetic change in the fetus.

Epigenetics refers to persistent changes in gene expression that result from various exposures, without change in the actual DNA code.

Epigenetic changes can affect an individual’s health for a lifetime and can be transmitted across generations.
Long-term health effects of air pollution

Emerging research suggests that air pollution is an important trigger for epigenetic change.

Effects on the developing fetal immune system.

Childhood allergies and asthma.

Hypothesis

The offspring born during the late 1980s in Utah Valley have now reached adulthood.

We hypothesize that prenatal exposure of these individuals to air pollution is associated with long-term health and reproductive consequences.

• Utah Population Database
• Sibling comparisons: account for shared genetic and environmental factors.
Study Aims

**Aim 1**: Identify a cohort of women (1<sup>st</sup> generation) with a pregnancy during the mill closure and a preceding or subsequent pregnancy during the mill operation.

**Aim 2**: Assess the relative risks between exposed (mill in operation) and unexposed (mill closed) offspring for adverse adolescent/adult health and reproductive outcomes (2<sup>nd</sup> generation).

**Aim 3**: Assess whether timing of exposure (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> trimester) to the mill closure modifies the risk for these adverse adult outcomes.

**Aim 4**: Assess whether offspring (3<sup>rd</sup> generation) of those individuals born during the mill operation are at increased risk for adverse birth outcomes (e.g. low birthweight).
Significance and future directions

Air pollution is a ubiquitous exposure in pregnancy.
The Geneva Steel Mill represents a unique, natural experiment.
Long-term, trans-generational health outcomes.
Rich resources of the UPDB.
Eventual contact with adults (and their children) born during the steel mill closure or operation:
• Obtain detailed health information, define phenotypes, and collect biospecimens for epigenetic analyses
Sample Sizes of the 5 Key Unexposed and Exposed Cohorts

<table>
<thead>
<tr>
<th>Cohort Description</th>
<th>Sample Size</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Unexposed</td>
<td>53571</td>
<td>66%</td>
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<tr>
<td>Exposed Older Sibs UT Co</td>
<td>11367</td>
<td>14%</td>
</tr>
<tr>
<td>Exposed Younger Sibs UT Co</td>
<td>7619</td>
<td>9%</td>
</tr>
<tr>
<td>Sibs Outside UT Co</td>
<td>7311</td>
<td>9%</td>
</tr>
<tr>
<td>All Other UT Co Births</td>
<td>1978</td>
<td>2%</td>
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</table>

The sample sizes represent counts of birth certificates and all the information they contain (e.g., birth weight, gestational age, complications).
Measures of Follow-Up in Utah: Proportion of Offspring with Utah Driver Licenses or Living in Utah at age 16

- Unexposed
- Exposed Older Sibs UT Co
- Exposed Younger Sibs UT Co
- Sibs Outside UT Co
- All Other UT Co Births

Bar chart showing proportions:
- Holds a UT Driver License
- Proportion in UT after age 16
Counts of Medical Records by Exposure Group:

- **Inpatient**
- **Amb Surgery**
- **IHC**
- **UUHSC**

<table>
<thead>
<tr>
<th>Exposure Group</th>
<th>Records</th>
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<tbody>
<tr>
<td>Unexposed</td>
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<tr>
<td>UT</td>
<td>49654</td>
</tr>
</tbody>
</table>
Number of Offspring of Generation Two

- Unexposed: 3242
- Exposed Older Sibs UT Co: 3830
- Exposed Younger Sibs UT Co: 875
- Sibs Outside UT Co: 493
- All Other UT Co Births: 13913
Deaths and Incident Cancers

- Unexposed: 154
- Exposed Older Sibs UT Co: 166
- Exposed Younger Sibs UT Co: 79
- Sibs Outside UT Co: 29
- All Other UT Co Births: 801
- Death Record: 216
- Utah Cancer Registry: 60

Thanks to Heidi Hanson and Jathine Wong!