Correlations between immunologic alterations and metal exposure within the Navajo Birth Cohort Study

Presented by Jennifer Ong and Shea McClain

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• NIEHS (16 yrs)
• CDC/ATSDR (5 yrs)
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• NIMHHD (4 yrs)
• NNEPA (1 yr)
• NiAAA (4 yrs)
• NIGMS K12 (3 yrs)
• UNM-COP
• UNM-CTSC
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• Many supporting chapters
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• NAIHS & PL-638 hospital laboratory staff, leadership, and health boards

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• DiNEH and NBCS Research is reviewed and monitored by Navajo Nation Human Research Review Board

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Exposure to uranium on Navajo

521 abandoned U mines; >1100 of 10,400 waste sites identified in western US
Multiple metals and metalloids
Multiple pathways:
Consumption of local water and crops,
Contact with contaminated soil and dust
Inhalation of metals released from combustion for home heating
Drinking water

Map of arsenic (A) and uranium (B) concentrations in Navajo Nation water sources and their proximity to mining areas

15% > MCL
13% > MCL
Presence of environmental metals

Dearth of toxicity knowledge

Unique exposure pathways

Disparities in care

Adverse health effects/health disparities

Immune system?
What is “immune system”? Complex network of cells and organs that work together to protect the body from infection

1) **Thymus**: Formation of T cells
2) **Tonsils/Adenoids**: Distinguish invaders for destruction
3) **Spleen**: Filters blood and distributes T and B cells
4) **Lymph Glands**: Storage and white blood cell formation
5) **Bone Marrow**: B cells are produced in bone marrow
When infections are present, the cells of the immune system work together to help eradicate the pathogen (such as bacteria or viruses).

Introducing some of the key players--

- **CD4 or “helper” cell**
  - Facilitates the activity of other immune cells

- **CD8 or “killer” cell**
  - Kills infected cells after activation by “helpers”

- **B cell**
  - Makes antibodies
  - Antibodies are produced after infection or vaccination and provide long-term protection

- **NK cells**
  - Kill cells that are infected or foreign (i.e. do not belong).
Significance
Toxicity to immune system can lead to adverse health outcomes

Environmental metal exposure??

Immune alteration/dysregulation

Immune Activation

Chronic inflammation

Autoimmune disease

Cancer

Immune Suppression

Chronic infection
Hypothesis- Chronic low-level environmental exposure to metal mixtures from contributes to immune system dysregulation.

To begin to address this complex question-we can measure immune cell populations to see if there are changes in the numbers of the different types of cells
Experimental Approach

- Measure lymphocyte populations from blood samples from NBCS mothers.

- Perform preliminary statistical analysis to determine if associations are seen between immune cell populations and the following metals as detected in the blood or urine from participants.

  - Metals: arsenic, cadmium, mercury, manganese, uranium and zinc
  - Statistical approaches: Spearman correlations and multivariable regression analysis
How do we measure different cell types?
Changes in cell populations are observed in association with metal exposures

<table>
<thead>
<tr>
<th>Cell population affected</th>
<th>Metal</th>
<th>Statistical Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total # of immune cells</td>
<td>Uranium, arsenic, manganese</td>
<td>Multivariable, Spearman (Mn)</td>
</tr>
<tr>
<td>Total # of T cells</td>
<td>Uranium, arsenic, cadmium</td>
<td>Multivariable</td>
</tr>
<tr>
<td># of activated CD4 cells (HELPER cells)</td>
<td>Cadmium</td>
<td>Multivariable</td>
</tr>
<tr>
<td># of CD8 cells (KILLER cells)</td>
<td>Cadmium</td>
<td>Multivariable, Spearman</td>
</tr>
<tr>
<td># of activated B cells (ANTIBODY Producing Cells)</td>
<td>Manganese</td>
<td>Multivariable, Spearman</td>
</tr>
<tr>
<td># of NK cells (NATURAL KILLER cells)</td>
<td>Uranium, arsenic, manganese, cadmium</td>
<td>Multivariable, Spearman (Mn)</td>
</tr>
</tbody>
</table>
Conclusions

• Several associations are seen between concentrations of metals and increases or decreases in immune cell populations in the blood of participants in the NBCS.

Importance

• Changes in populations of immune cells can lead to changes in immune functions.
• Immune dysregulation can lead to increased infections, autoimmune responses, and cancer.
Next Steps

• Examine immune cell data along with other immune system markers
• Consider the effects of metal mixtures on these populations
• Incorporate demographics, dust, and survey data into statistical modeling to see if there are significant differences in immune cell populations based on this information