Webinars
Series of scientific webinars that provide a forum for discourse on scientific issues.
Live and On-Demand
Case Conferences
Journal Clubs
Grand Rounds
CE Available

Online Courses
Evidence-based online courses on a variety of children’s environmental health topics.
Interactive and Self-Paced
CE Available

Resource Catalog
Fact sheets, journal publications, reports, and other resources for parents, community members, patients and healthcare professionals
Topics included:
Air Quality, Pesticides, Natural Disasters, BPA, Mold, Lead, Mercury
A National Alliance of Scientists, Health Professionals and Environmental Health Advocates.

Co-Founded & Co-Directed by Maureen Swanson, Learning Disabilities Association, and Dr. Irva Hertz-Picciotto, UC Davis.
Scientific evidence at a tipping point: Toxic chemicals play a role in neurodevelopmental disorders.

Learning, developmental, intellectual disabilities affect 1 in 6 children in U.S.

Increasing prevalence of autism spectrum disorder, ADHD.
Project TENDR Mission

- To protect pregnant women and children from toxic chemicals and pollutants that harm brain development, **by joining scientific evidence with advocacy**

- To inform and empower change makers **to create policies ensuring that no child is exposed to chemicals and pollutants that contribute to neurodevelopmental disorders.**
Project TENDR: Two pronged approach

- Published a *Consensus Statement*—2016 in Environmental Health Perspectives
- New York Times, CNN, NPR, 100s of smaller media outlets.

- Target a short list of neurotoxic chemicals that highlight the larger problem of toxicants in the environment.
- Address systemic problems in chemical regulatory policies and implementation.
Prime example chemicals and pollutants that increase children’s risks for neurodevelopmental disorders

- Lead
- Organophosphate pesticides
- Polybrominated diphenyl ethers (flame retardants)
- Air pollution
- Phthalates (emerging concern)

Scientific evidence of harm.
Exposure widespread.
Reduction of levels is feasible.
Exposure by ingestion or inhalation:
- Peeling paint in older houses
- Lead water pipes
- Lead battery recycling
- Aviation gas, cosmetics, bullets, etc.

- There is no safe level of lead for children.

Over 150 years of documented effects on children.

Loss of IQ, developmental delays, ADHD, learning disabilities.

Opportunities for exposure reduction:
- cleaning up or replacing soil, chipped paint, water pipes; banning lead from products; ensuring no new uses of lead.
Ensure that no child has a blood lead level $>5 \, \mu g/dL$ (>50 ppb) by 2021.

Eliminate lead exposures to pregnant women and children so that by 2030, no child would have a blood lead level $>1 \, \mu g/dL$ (>10 ppb).

Project TENDR’s Recommendations to achieve these goals

- adopted by the American Medical Association, verbatim, in December 2016,
- Published in *JAMA Pediatrics* in May, 2017
Project TENDR: Organophosphate Pesticides

- Exposure through:
  - Household pest control
  - Occupations in agriculture
  - Residues on foods
  - Drift from agricultural applications

- Associations with cognitive impairments (i.e., decreased IQ), autism, & symptoms of ADHD
- Changes in brain function found on MRI
- Opportunities for exposure reduction through non-toxic alternatives, organic farming, washing fruit with no peel

Project TENDR’s Recommendations to eliminate OP pesticides
Published in PLoS Medicine in October, 2018
Project TENDR: Air Pollution

- Widespread exposure, largely due to motor vehicle traffic
- Literature shows deficits in cognitive skills, risks for ASD
- Supported by animal experiments
- Adds to known respiratory effects
- Opportunities for exposure reduction:
  - Public transportation
  - More bicycle and pedestrian-friendly city planning
  - Technologic advances – hybrids, all-electric vehicles

Project TENDR’s Recommendations to reduce air pollution
Published in Amer J Public Health in March, 2019
Process: First the Evidence

- **TENDR work group articles, recommendations**
  - A national strategy on lead, *JAMA Pediatrics* 2017
  - Organophosphate pesticides: nerve agents *PLoS Med* 2018
  - Healthy air for healthy minds, *Am J Pub Health* 2019

- **Work groups underway:** PBDEs and phthalates

- **New work groups in 2019**
  - Climate change and neurodevelopment
  - Disproportionate exposures/health disparities
  - Autism & environmental factors

- **Collaboration with advocacy organizations**
Process: Then the Action

- Congressional briefings
- **Comment letters** on federal, state and international policies & proposed rules.
- Op-eds
- Providing **Expert Testimony** on the science
  - Federal agency rulings on PBDEs, lead
  - State bills on toxic chemicals in children’s products, and on neurotoxic pesticides
  - Amicus brief in case on federal phthalates rule
- **Grand rounds and professional presentations**
Project TENDR is working for a future where all children are no longer exposed to harmful chemicals, and where we have eliminated the disproportionate exposure for children of color and families of low-income. Our children live in a clean, safe and healthy world. They can and do realize their full potential.
Thank you!

ihp@ucdavis.edu
Healthy Air, Healthy Brain: Emerging Evidence Streams and Advancing Air Pollution Policy to Protect Children’s Health

Melanie Marty, PhD
Assistant Deputy Director (Retired)
Office of Environmental Health Hazard Assessment, California EPA
PEHSU Region 9
Acknowledgements

This work was supported by **Project TENDR** (Targeting Environmental Neurodevelopmental Risks)

- Commentary in American J Pub Health, Feb 21, 2019
- Authors: Devon Payne-Sturges, DrPH, Melanie A. Marty, Ph.D., Frederica Perera, DrPH, PhD, Mark D. Miller, M D, Maureen Swanson, MPA, Kristie Ellickson, PhD, Deborah A. Cory-Slechta, PhD, Beate Ritz, MD, PhD, John Balmes, MD, Laura Anderko, RN, PhD, Evelyn O. Talbott, DrPH, Robert Gould, MD, and Irva Hertz-Picciotto, PhD, MPH

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DISCLAIMER: The material presented does not represent an official position of CalEPA or the Office of Environmental Health Hazard Assessment
Learn about emerging evidence of combustion-related air pollution effects on the developing brain from epidemiological and animal toxicology studies and potential mechanisms of action.

Understand more about the regulatory paradigm governing air pollution in the U.S.

Hear some policy recommendations from TENDR
Combustion-related Air Pollution

Defined for our purposes as:

- fine particulate matter (PM2.5, including ultrafine particulate matter; ≤100 nm)
- polycyclic aromatic hydrocarbons
- nitrogen dioxide
- other pollutants for which nitrogen dioxide and PM2.5 are markers.
Neurodevelopmental Effects of Air Pollution

- First, air pollution (measured as PM, NO$_2$, and other metrics) is associated with preterm birth, lower birth weight, and term low birth weight (<2500 g)

- These adverse birth outcomes are risk factors for neurodevelopmental deficit including longer-term motor, cognitive, visual, hearing, behavioral, social-emotional health
What do we mean by PM?
Air Pollution and Pre-term Birth

- Exposure to particulate matter and ozone over the entire pregnancy was significantly associated with higher risk for preterm birth (<37 weeks gestation)
- Pooled effect estimates:
  - $1.09 \ (1.03-1.16)$ per $10 \mu g/m^3$ increase in PM$_{10}$,
  - $1.24 \ (1.08-1.41)$ per $10 \mu g/m^3$ increase in PM$_{2.5}$,
  - $1.03 \ (1.01-1.04)$ per 10 ppb increase in ozone.
Meta-analysis PM and birthweight
(Figure 2 Lamichhane et al 2015)

Note: weights are from random effects analysis
Meta-analysis PM and birth weight

- For PM$_{10}$, pooled smoking adjusted estimate for the entire pregnancy,
  \[ ES = -10.31 \text{ g (-13.57 to -7.05)} \]

- For PM$_{2.5}$, the pooled smoking-adjusted estimate was greatest for the entire pregnancy
  \[ ES = -22.17 \text{ g (-37.99 to -6.41)} \]
## Multi-country meta-analysis of PM2.5 and term LBW (Dadvand et al EHP 2013)

<table>
<thead>
<tr>
<th>PM2.5 – meta-analysis of data from 7 centers</th>
<th>OR (95% CI) Per 10µg/m3 PM2.5</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>1.17 (1.08, 1.26)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Adjusted – maternal SES</td>
<td>1.10 (1.03, 1.18)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Adjusted – maternal SES and center specific co-variates</td>
<td>1.04 (0.99, 1.09)</td>
<td>0.09</td>
</tr>
</tbody>
</table>
A growing body of human studies associate exposure to combustion-related air pollutants (PM2.5, polycyclic aromatic hydrocarbons, nitrogen dioxide, black carbon) with adverse effects on brain development, including deficits in intelligence, memory, and behavior.

Other studies have linked roadway proximity, traffic-related PM, elemental carbon (a measure of soot), or nitrogen dioxide (formed during combustion) to decreased cognitive function, including deficits in memory and attention.

## Sampling of studies

<table>
<thead>
<tr>
<th>Prospective Cohort Studies</th>
<th>Sample characteristics</th>
<th>Measurement of air pollution</th>
<th>Measurement of cognition</th>
<th>Confounders assessed</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suglia et al., 2008</td>
<td>N = 202; age 8-11 yrs</td>
<td>Quartiles of average black carbon</td>
<td>Cognitive functioning, K-BIT, WRAML</td>
<td>Age, gender, primary language, mother’s education, tobacco smoke exposure in utero, ETS exposure, birth weight, blood lead level</td>
<td>0.4 ug/m3 increase in black carbon predicted decreased scores: K-BIT Matrices (-4.0, -7.6 to -0.5); Composite (-3.4, -6.6 to -0.3); Visual (-5.4, -8.9 to -1.9); WRAML Learning (-2.8, -6.6 to 1.1); General index (-3.9, -7.5 to -0.3).</td>
</tr>
<tr>
<td>Jedrychowski et al, 2015</td>
<td>N= 170; age 7 yrs</td>
<td>Household airborne PAH</td>
<td>Verbal IQ, WISC-R</td>
<td>Birth season, birth season X cord blood adducts, maternal education, gender, parity, breastfeeding duration</td>
<td>1-unit increase in PAH (logtransformed) associated with increased risk of depressed verbal IQ: RR 1.6 (1.1–2.5) p&lt;0.027</td>
</tr>
<tr>
<td>Harris et al (2015)</td>
<td>N = 1109; mean 8 yrs;</td>
<td>Proximity of residence to nearest major roadway/near residence traffic density.</td>
<td>Verbal and non-verbal IQ, visual motor, design and picture memory; WRAML2, KBIT-2, WRAVMA</td>
<td>income, HOME, maternal IQ, sex, age, breastfeeding, maternal age, marital status, parental education, race, smoking, ETS in utero, blood lead in utero and early childhood, pre-natal alcohol, gas stove</td>
<td>lower nonverbal IQ [-7.5 points; 95% confidence interval (CI): -13.1, -1.9], and somewhat lower verbal IQ (-3.8 points; 95% CI: -8.2, 0.6) and visual motor abilities (-5.3 points; 95% CI: -11.0, 0.4)</td>
</tr>
</tbody>
</table>
Polycyclic aromatic hydrocarbons, a component of PM2.5, have been associated with:
- developmental delay;
- reduced IQ;
- symptoms of anxiety, depression, and inattention;
- ADHD; and
- reduced size of brain regions important for processing information and impulse control.

High maternal blood PAH-adducts significantly associated with:

- Conner’s Parent Rating Scale-Revised DSM-IV Inattentive (OR = 5.06, 95% CI [1.43, 17.93])
- DSM-IV Total (OR = 3.37, 95% CI [1.10, 10.34]) subscales.
Increasing evidence links prenatal exposure to traffic-related air pollutants and PM2.5 to autism spectrum disorder.

Some studies find associations between early postnatal exposure to PM2.5 and development of autism spectrum disorder or Asperger's.

### Raz et al., 2015

**PM2.5 and autism spectrum disorder**

<table>
<thead>
<tr>
<th>Quartile of PM2.5</th>
<th>OR(^a) (95% CI) for ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>second</td>
<td>1.65 (0.98-2.8)</td>
</tr>
<tr>
<td>third</td>
<td>1.84 (1.07-3.17)</td>
</tr>
<tr>
<td>fourth</td>
<td>2.06 (1.17-3.63)</td>
</tr>
<tr>
<td>Per Interquartile range</td>
<td>1.63 (1.08-2.47)</td>
</tr>
</tbody>
</table>

Cases = 160; matched controls = 968 (nested case-control, Nurses’ Health Study II cohort)

\(^a\) adjusted for child sex, year of birth, month of birth, maternal and paternal age at birth, census income
Ritz et al (2018) autism and postnatal air pollution

Estimated PM (2.5 and 10), NO$_2$ and SO$_2$ at residence

Adjusted ORs for ASD per interquartile range (IQR) increase for 9 month after pregnancy:

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO$_2$</td>
<td>1.08 (95% CI: 1.01, 1.15)</td>
</tr>
<tr>
<td>PM2.5</td>
<td>1.06 (95% CI: 1.01, 1.11)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.04 (95% CI: 1.00, 1.09)</td>
</tr>
<tr>
<td>SO$_2$</td>
<td>1.21 (95% CI: 1.13, 1.29)</td>
</tr>
</tbody>
</table>
Prenatal exposures to fine and ultrafine combustion particles in mouse models produced:

- Structural alterations
- Hypermyelination
- Inflammation in fetal brain
- Altered region-specific neurotransmitter content (dopamine and norepinephrine)
- In males as adults, decreased activity, increased anxiety, and brain microglial activation

Postnatal exposures of mice to concentrated urban ultrafine particles (similar to exposures in high traffic areas of major cities) demonstrated:

- Disrupted development of the corpus callosum
- Elevated brain glutamate levels (an excitatory neurotransmitter) that persist into adulthood
- Impaired learning and short-term memory
- Increased impulsivity

Fine and ultrafine PM Neuroinflammation

Inhaled particles
Olfactory bulb via olfactory epithelium
Enter systemic circulation and cross BBB
Increase inflammatory cytokines and ROS
Neurodevelopmental deficits
Neuronal injury and loss
Other Potential Mechanisms of Action

- Altered methylation of DNA observed in brains of humans with ASD and animal models of air pollution developmental neurotoxicity; could alter gene expression
- Expression of reelin – signaling glycoprotein during neurodevelopment (neuronal migration and polarity) and in adults modulates learning and memory- is dysregulated in mice exposed to fine PM from diesel engines and in people with ASD.

Clean Air Act is the major air pollution law in the U.S.
Many activities of USEPA are enabled by this key legislation.
Federal EPA sets standards for criteria air pollutants

- PM, NO$_2$ and ozone reductions are driven by associations with mortality in the elderly
- To date have not considered benefits to or costs of neurodevelopmental deficits.
A “Pyramid of Effects” from Air Pollution

- Death
- >90% of monetized benefits
- ER visits, Hospital admissions, Heart attacks
- Doctor visits, School absences, Lost work days
- Respiratory symptoms, Medication use, Asthma attacks
- Lung function decrements, Inflammation, Cardiac effects

Magnitude of Impacts

Severity of Effects

Proportion of population affected
TENDR Recommendations

- Recommendation 1: The US Environmental Protection Agency (EPA) should give greater consideration to the evidence on the effects of air pollutants on neurodevelopment when setting standards for combustion-related air pollutants and when assessing the full cost of the health effects of air pollution.
Recommendation 2: Strengthen and enforce federal fuel efficiency standards.

- Fuel economy standards issued by the EPA and the National Highway Traffic Safety Administration
- Fuel economy of new vehicles will increase from an average of about 25 miles per gallon today to about 36 miles per gallon
  - Translates to ~2000 fewer gallons of gas burned over a typical vehicle lifetime and lower emissions.
Recommendation 3: Promote and advance clean energy policies that reduce reliance on fossil fuels, including coal, combusted for energy generation and transportation.

Obvious reductions in combustion-related air pollution
Recommendation 4: Target existing large sources of combustion-related air pollutants for emissions reductions, dramatically reducing exposures in neighboring communities.
Consider where sources are allowed

Recommendation 5: Regional air pollution control agencies across the United States should restrict permitting new sources of combustion-related air pollutants in close proximity to residential areas and other sensitive receptors.

April 2005
California Environmental Protection Agency
California Air Resources Board

AIR QUALITY AND LAND USE HANDBOOK: A COMMUNITY HEALTH PERSPECTIVE
More monitoring near children

Recommendation 6: Expand air monitoring near locations where children spend time. Most monitors meant to capture average exposures, not high-end. Not near highly burdened communities.
Mitigate Near Source Exposures

Recommendation 7: Expand research on effectiveness of strategies to mitigate exposures near large sources of combustion-related air pollution that could guide implementation in neighborhoods close to such sources.

California Air Resources Board
Reducing Near Roadway Exposure to Air Pollution
https://ww2.arb.ca.gov/resources/documents/research-synthesis-17-03-reducing-near-roadway-exposure-air-pollution
Recommendation 8: Increase research on the human health effects of ultrafine particles.

From: Big Road Blues
https://now.tufts.edu/articles/big-road-blues-pollution-highways
Disclaimer: This material was supported by the American Academy of Pediatrics (AAP) and funded (in part) by the cooperative agreement FAIN: 5 NU61TS000237-05 along with the American College of Medical Toxicology and funded (in part) by the cooperative agreement FAIN: 5U61TS000238-05 from the Agency for Toxic Substances and Disease Registry (ATSDR).

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