The Children’s Health Study

Ed Avol
Department of Preventive Medicine
avol@usc.edu
Today’s Talk

Overview of:
Children’s Health Study (CHS)
CHS Design, Direction, and Results

“To Infinity…
…and Beyond!”
(CHS Future Plans)
Children’s Health Study (CHS)

- a “10-year” longitudinal study (est. 1992)

- Conducted by the University of Southern California (USC)

- Supported by the California Air Resources Board (CARB), USEPA, NIEHS, NHLBI, & the Hastings Foundation
Don’t we already know air pollution is bad for us?
Does air pollution cause permanent health effects?
• Long-term outdoor exposure & respiratory health outcomes
  – Lung development
  – Respiratory symptoms
  – Asthma

• Identify specific pollutants
Why Children?

• **Exposure**
  - They spend more time outdoors
  - They are more active

• **Physiology**
  - They have higher ventilation rates
  - They have different lung deposition patterns
  - They are still growing

• **Complications (Confounders)**
  - They don’t have occupational exposures
  - They don’t smoke (…we hope)

• **Logistics**
  - You can find a lot of them in schools!
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>938</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td>937</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>1,806</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>2,081</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>5,603</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11,365</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cohort E includes kindergarten (K) grades.
Southern California has a wide range of many pollutants found in the U.S.
A Pollutant “Package”?

Table 1. Correlation of Mean Air-Pollution Levels from 1994 through 2000 across the 12 Study Communities.*

| Pollutant       | O₃ (10 a.m.–6 p.m.) | NO₂ | Acid Vapor† | PM₁₀  | PM₂.₅ | Elemental Carbon | Organic Carbon |
|-----------------|---------------------|-----|-------------|-------|-------|-----------------|----------------
| O₃              | 0.98                | 0.10| 0.53        | 0.31  | 0.33  | 0.17            | 0.25           |
| 1-Hour maximal level | -0.11              | 0.35| 0.18        | 0.18  | -0.03 | 0.13            |                |
| 10 a.m.–6 p.m.  |                     |     |             |       |       |                 |                |
| NO₂             |                     |     |             |       |       |                 | 0.87           |
| Acid vapor†     |                     |     |             |       |       |                 | 0.79           |
| PM₁₀            |                     |     |             |       |       |                 | 0.79           |
| PM₂.₅           |                     |     |             |       |       |                 | 0.95           |
| Elemental carbon|                     |     |             |       |       |                 | 0.85           |
| Organic carbon  |                     |     |             |       |       |                 | 0.91           |
In Southern California, a primary source of exposure is ...
...vehicle exhaust involves more than cars...
Average FEV$_1$ over 5 years
4$^{th}$ grade (Cohort C), 1993-1997

On average, FEV$_1$ increased about 12% per year...
(~25 to 30ml per month; you can almost see them grow!)
Lung function growth vs. NO$_2$
Cohort C: 1993-1997

Annual FEV$_1$ Growth (%)

NO$_2$ (ppb)

R = -0.60
p = 0.025

Gauderman et al. 2000
...But what happens to lung growth if a child moves?

Some move to higher pollution, some to lower...
Lung Growth Rate Changes seem reversible...during adolescence
What about longer-term growth?

FEV₁ Growth Over 8 Years

Girls

Boys
Yes, Pollution Slows Lung Function Growth

Gauderman et al., 2004
Pollution Effects on 8-yr Growth

- 8-year lung growth deficits associated with:
  - NO₂, Acid vapor, PM₂.₅, Elemental Carbon
- Associations in all types of kids, including:
  - Boys and girls
  - Non-asthmatics
  - Non-smokers
- No associations with ozone
Why are Annual Growth Rates Important?

Increased risk of:
- Cardiovascular disease
- Respiratory disease
- Mortality
Are These Observations “Clinically Significant”?

(Clinically Significant = Below 80% of “normal”)

Girls

Boys

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>FEV1 (milliliters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1000</td>
</tr>
<tr>
<td>10</td>
<td>2000</td>
</tr>
<tr>
<td>12</td>
<td>3000</td>
</tr>
<tr>
<td>14</td>
<td>4000</td>
</tr>
<tr>
<td>16</td>
<td>5000</td>
</tr>
<tr>
<td>18</td>
<td>6000</td>
</tr>
<tr>
<td>20</td>
<td>7000</td>
</tr>
</tbody>
</table>

4th Grade → 12th

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>FEV1 (milliliters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1000</td>
</tr>
<tr>
<td>10</td>
<td>2000</td>
</tr>
<tr>
<td>12</td>
<td>3000</td>
</tr>
<tr>
<td>14</td>
<td>4000</td>
</tr>
<tr>
<td>16</td>
<td>5000</td>
</tr>
<tr>
<td>18</td>
<td>6000</td>
</tr>
<tr>
<td>20</td>
<td>7000</td>
</tr>
</tbody>
</table>

4th Grade → 12th
18yr-olds living in polluted communities are four to five times more likely to have abnormally low lung function.

\[ R = 0.79 \quad P = 0.002 \]
Low PFTs Associated with Many Pollutants

O$_3$

- FEV$_1$ < 80% Predicted vs. 10 am - 6pm O$_3$ (ppb)
- R = 0.75, P = 0.005

PM$_{10}$

- FEV$_1$ < 80% Predicted vs. PM$_{10}$ (μg/m$^3$)
- R = 0.66, P = 0.02

NO$_2$

- FEV$_1$ < 80% Predicted vs. NO$_2$ (ppb)
- R = 0.79, P = 0.0002

PM$_{2.5}$

- FEV$_1$ < 80% Predicted vs. PM$_{2.5}$ (μg/m$^3$)
- R = 0.69, P = 0.01

Acid

- FEV$_1$ < 80% Predicted vs. Acid Vapor (ppb)
- R = 0.69, P = 0.01

EC

- FEV$_1$ < 80% Predicted vs. Elemental Carbon (μg/m$^3$)
- R = 0.74, P = 0.006
Particle Number Concentration and Distance from Busy Roadways

Zhu et al 2003
## 8yr Growth & Traffic

<table>
<thead>
<tr>
<th>Community</th>
<th>N</th>
<th>&lt;500</th>
<th>500-1000</th>
<th>1000-1500</th>
<th>&gt;1500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riverside (RV)</td>
<td>329</td>
<td>103</td>
<td>66</td>
<td>61</td>
<td>99</td>
</tr>
<tr>
<td>Atascadero (AT)</td>
<td>278</td>
<td>83</td>
<td>60</td>
<td>46</td>
<td>89</td>
</tr>
<tr>
<td>Alpine (AL)</td>
<td>308</td>
<td>81</td>
<td>54</td>
<td>42</td>
<td>131</td>
</tr>
<tr>
<td>San Dimas (SD)</td>
<td>293</td>
<td>47</td>
<td>145</td>
<td>83</td>
<td>18</td>
</tr>
<tr>
<td>Long Beach (LB)</td>
<td>320</td>
<td>54</td>
<td>64</td>
<td>54</td>
<td>148</td>
</tr>
<tr>
<td>Santa Maria (SM)</td>
<td>310</td>
<td>44</td>
<td>74</td>
<td>58</td>
<td>134</td>
</tr>
<tr>
<td>Mira Loma (ML)</td>
<td>319</td>
<td>9</td>
<td>30</td>
<td>45</td>
<td>235</td>
</tr>
<tr>
<td>Lancaster (LN)</td>
<td>315</td>
<td>3</td>
<td>35</td>
<td>31</td>
<td>246</td>
</tr>
<tr>
<td>Lake Elsinore (LE)</td>
<td>306</td>
<td>12</td>
<td>17</td>
<td>7</td>
<td>270</td>
</tr>
<tr>
<td>Upland (UP)</td>
<td>283</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>279</td>
</tr>
<tr>
<td>Lompoc (LM)</td>
<td>281</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>281</td>
</tr>
<tr>
<td>Lake Arrowhead (LA)</td>
<td>335</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>335</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3,677</td>
<td>440</td>
<td>545</td>
<td>427</td>
<td>2,265</td>
</tr>
</tbody>
</table>
# 8-Yr Growth vs. Distance to Freeway

<table>
<thead>
<tr>
<th>Traffic Indicator</th>
<th>$\text{FEV}_1$ (ml)</th>
<th>Diff</th>
<th>(95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freeway distance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 500 m</td>
<td>-80.6</td>
<td>(-143.3, -17.8) *</td>
<td></td>
</tr>
<tr>
<td>500 - 1,000 m</td>
<td>-41.0</td>
<td>(-98.9, 16.9)</td>
<td></td>
</tr>
<tr>
<td>1,000 - 1,500 m</td>
<td>-33.2</td>
<td>(-92.7, 26.3)</td>
<td></td>
</tr>
</tbody>
</table>

* $p<0.05$ relative to >1,500 m from a freeway

Gauderman et al 2007
Freeway-related Growth Deficits

• Independent of:
  – Socio-economic status
  – Smoking and second-hand smoke
  – Asthma status

• Just an L.A. problem?...NO
  – Freeway proximity is important even if overall air quality is good
Combined Effects of Regional & Local Exposure on 8-yr FEV₁ Growth

Regional PM₂.₅ & Freeway Distance

- Low PM₂.₅ & Far from Fwy
- Low PM₂.₅ & Near Fwy
- High PM₂.₅ & Far from Fwy
- High PM₂.₅ & Near Fwy

Lung Function Growth

86% 88% 90% 92% 94% 96% 98% 100%
Air Pollution affects school absences...and more

- 20 ppb change in ambient O$_3$
- 83% increase in acute respiratory school absences

Lost school learning time, parental work time, doctors’ visits, medication...
Cumulative (LA Basin) annual cost of absences:

$\sim$200,000,000 !!!

(Gilliland et al, 2001)

(Hall et al, 2003)
Children’s Health Study

- Are there vulnerable sub-populations?
- Can they be identified and characterized?
Air Pollution & Asthma

(McConnell, et al., 1999)
Ozone Modifies the Effect of Sports on New Onset Asthma

Average Ozone from 10a.m.-6p.m.(1994-1997)

Relative Risk of Asthma/Team Sport

0.5 0.7 0.9 1.1 1.3 1.5 1.7 1.9 2.1

25 35 45 55 65 75

(McConnell et al, 2002)
Prevalent Asthma & Distance to a Major Road Among Long-Term & Short-Term Residents (Cohort E)

Figure 2. Prevalence of asthma by distance of residence to a major road within 500 m, among long-term (A) and short-term (B) residents with no family history of asthma. Dotted lines indicate 95% confidence interval.
Adding Genes to the Mix

...a biological hypothesis (e.g. Gilliland et al.)

- Oxidative Product Detoxification
- Respiratory Outcomes
- ROS Metabolism
- Molecular and Enzymatic Antioxidants
- Inflammation
- Oxidative Stress
- Xenobiotic Metabolism
- Air Pollution
Schools still rise close to freeways
L.A. Unified continues to build near roads that spew pollution despite a state law and evidence of health hazards.
By Evelyn Larrubia
Los Angeles Times Staff Writer

September 24, 2007

Despite a state law that seeks to prevent schools from being built near freeways and mounting evidence that road pollutants harm children's lungs, the Los Angeles Unified School District is in the process of adding seven new schools to the more than 70 already located close to highways.

Board acts to limit new schools near freeways
L.A. Unified officials will have to do more to reduce students' exposure to airborne pollution.
By Evelyn Larrubia
Los Angeles Times Staff Writer

January 23, 2008
Inter-modal Trade Volume

Double digit growth Impact on Ports

LA/ LongBeach/Ports
2006 Stats
- 14.8 M TEU’s
- 65% Transferred to Inland Ports

Source: Double Stack Container Systems: Implications for US Railroads and Ports (Washington: US Department of Transportation)
• High vs. low pollution communities
  – Lower lung function
  – Increased symptoms
  – Increased asthma
• A “package of pollution” (combustion exhaust?) associated with slow lung growth
• Ozone fluctuations associated with school absence (acute respiratory disease)
• New cases of asthma associated with exercise in high ozone communities (a causal role?)
• Changes in air quality can influence lung growth rates (during adolescence, at least)
...(even more) CHS Conclusions...

- Children are a susceptible (& vulnerable) group
  - Rapid (and responsive) growth
  - Proximity to exposure

- Regional & local exposures matter
...ever more CHS Conclusions...

- Vulnerable subgroups
  - Asthmatics
  - Genetic susceptibilities

- Traffic Proximity
  - Traffic density
  - “Big roads”
  - Combustion exhaust
CHS Conclusions (...so many!)

Are we “finished” yet?

Of Course Not!

• Still to Come:
  – Which pollutant is it, really?
  – Improved understanding of GxE interactions
  – Unraveling near-road/traffic proximity effects
  – To adulthood…and beyond!
  – To birth-hood…and before!
  – Better exposure assessment (up close & personal!)
  – The grand unification theory
CHS^n: It keeps going and going and going...

- Meanwhile, we’re still at it …
- Things to remember:
  - These results were observed at recent & generally declining levels of ambient pollution (BELOW CURRENT CLEAN AIR STANDARDS)
  - No apparent thresholds observed
  - Reductions in air pollution will likely lead to measurable improvements in health
USC Field Teams
Steve Howland
Lupe Valencia
Milena Lopez
Rudy Caldera
Letty Caldera
Lisa Grossman
Linda Smith
Julie Hulett
Gilbert Ramos
Andrea Nunez
Henry Valencia
Reshama Damle
Ned Realiza
Reyna Diaz
Susie Hutfless
Nadia Lupercio
Jeanine Hanna
Deborah Kim
Lori Nasi
Christine Fust
Cindy Woo
Dana Takamoto

USC Staff
Jun Manilla
Hita Vora
Josh Millstein
John Molitor
Jassy Molitor
Allison Padilla
Sylvia Tan
Talat Islam
Towhid Salam
Made Wenten

Sonoma Technology, Incorporated

Rancho Los Amigos Medical Center / LAREI

Aerosol Dynamics, Inc

South Coast Air Quality Management District

San Diego Air Pollution Control District

San Luis Obispo/Tri-Counties Air Pollution Control District

Mojave Air Pollution Control District

Antelope Valley Air Pollution Control District

California Air Resources Board
Thank you...any questions?