Chronic Air Pollution Exposure and Adverse Effects on the Brain: A Review

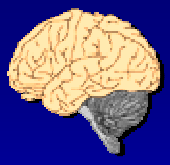
December 6, 2007

Air Resources Board

California Environmental Protection Agency

Thank you Mr. Goldstene. Good morning, Chairman Nichols and members of the Board. In this health update, I will provide a brief summary of recent preliminary findings of adverse effects on the brain associated with long-term exposure to air pollution.

Background



- Air pollution exposure associated with premature death, hospitalizations, and other adverse health effects
- Knowledge of air pollution effects on brain is limited
- Focus of this health update is a review of findings* on the effects of air pollution exposure on the brain

*Calderón-Garcidueñas L, Franco-Lira M, Torres-Jardón R *et al*. 2007. *Toxicologic Pathology* 35(1):154-62.

Funded by US Environmental Protection Agency, National Science Foundation, Montana Board of Research and Commercialization Technology, National Center for Research Resources (National Institutes of Health)

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In previous health updates, the Board has heard about numerous adverse health effects associated with exposure to air pollution. For example, air pollutant exposure has been linked to premature death, hospitalizations for respiratory and cardiovascular conditions, asthma symptoms, acute bronchitis, and atherosclerosis. These health outcomes are the result of effects on the heart, circulatory system and lungs. However, air pollutants may affect other organs of the body such as the brain. Information on the effects of air pollutants on the brain is just now coming to light, and today we will summarize findings discussed in a recent review article by Calderón-Garcidueñas and colleagues.

Air Pollutants' Potential Routes to the Brain

- May physically enter brain (ultrafine PM)
  - Transported along nerves in the nasal passages to brain
  - Carried from lungs to brain via bloodstream
- May affect brain indirectly (PM2.5 and ozone)
  - Inflammatory factors released in lungs, travel to the brain

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Although inhaled pollutants can exert adverse effects directly on the lungs and heart, the healthy brain is well-protected against toxins by a specialized membrane that usually allows entry only to beneficial substances. However, recent studies suggest that inhaled ultrafine particles may be capable of bypassing this barrier.

It is possible that inhaled particles may be transported along nerves that travel directly from the nasal passages into the brain, as shown in this simplified schematic figure. The white line represents the pathway of inhaled particles.

Another possibility is that ultrafines may enter the brain by a more circuitous route, by inhalation into the lungs and subsequent transport via the bloodstream, shown here in red, into the brain.

Alternatively, air pollutants may be able to exert effects on the brain without actually gaining entry to it. Inhaled pollutants, such as fine particulates and ozone, may cause an inflammatory reaction in the lung. This in turn may result in chemical factors being released into the bloodstream and subsequently being transported to the brain, as seen here, where the dashed green line represents the route of the inflammatory chemical factors.

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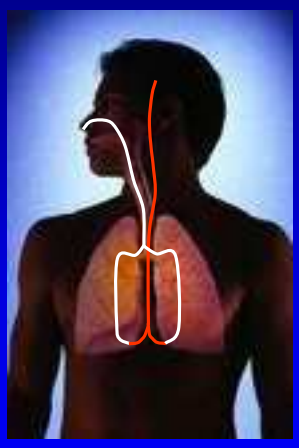

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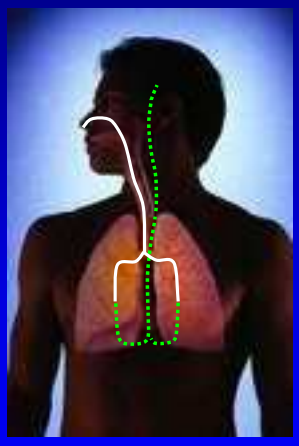

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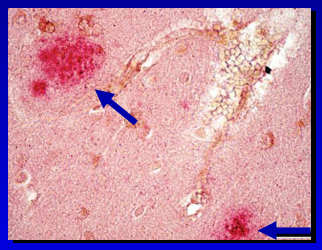
Chronic Air Pollution Exposure Associated with Brain Inflammation and Damage

- Brains of accidental death victims (adults and children) and healthy dogs compared between high- vs. low- pollution cities
  - Higher levels of inflammatory markers
  - Abnormal protein deposits
    - These changes may precede brain abnormalities seen in Alzheimer's disease



- In mice, exposure to concentrated ambient particles may increase likelihood of developing brain inflammation*

*Campbell A, Oldham M, Becaria A, Bondy SC, Meacher D, Sioutas C, Misra C, Mendez LB, Kleinman M. 2005. *Neurotoxicology* 26(1): 133-40.

Funded by CA Air Resources Board, National Institutes of Health, Southern California Particle Center and Supersite (US EPA)

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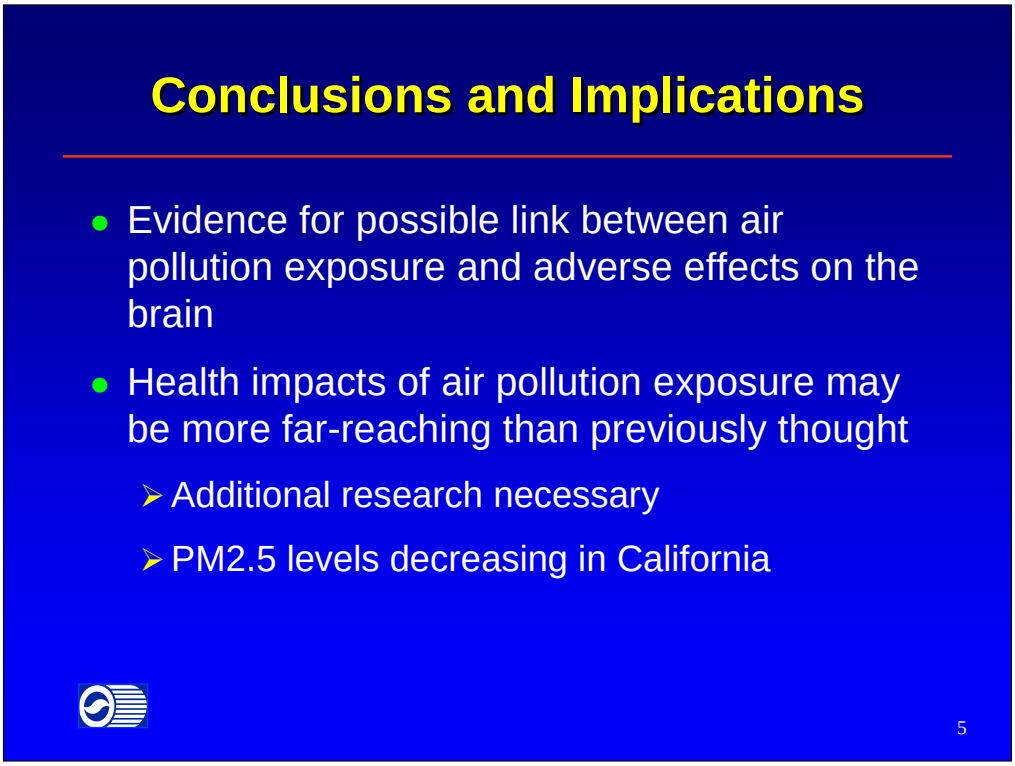
Evidence of the effects of chronic air pollution on the brain comes from several studies performed in Mexico. Researchers compared the brains of accidental death victims, both adults and children, from cities with highly polluted ambient air versus cities with relatively clean air. Similar studies were performed on healthy domestic dogs. The more polluted cities typically had ozone and particulate matter levels above our national ambient air quality standards. The results of these studies showed that levels of inflammatory markers and abnormal protein deposits were higher in the brain tissue of those from the highly-polluted versus the relatively clean cities. Both of these changes resemble those that typically precede Alzheimer's disease. However, these changes do not necessarily imply the onset of disease.

The figure on the right side of this slide shows brain tissue from a 36-year old man from Mexico City. Arrows point out locations of abnormal protein deposits. In a normal healthy brain, the tissue would appear more uniform in color and texture.

In a separate study conducted in Los Angeles by Campbell and colleagues, brains of mice exposed to concentrated ambient particles showed elevated levels of chemical markers that may precede inflammation. This suggests that particulate matter is the component in the air pollution mix responsible for the increases in inflammatory markers seen in the studies conducted in Mexico.



In conclusion, the studies discussed today suggest that air pollution exposure may be associated with adverse effects on the brain in both humans and animals. These effects include increased levels of inflammatory markers and abnormal protein deposits in brain tissue, and the results suggest that both adults and children may be at risk.

These findings also suggest that adverse health effects related to air pollution exposure may be more far-reaching than previously thought. Therefore, it is important that these linkages be rigorously investigated through additional research.

On a positive note, levels of ambient PM are decreasing in California. However, results such as those presented today illustrate that continued reductions of both gaseous and particulate pollution are needed to protect public health.

This concludes the Health Update; we will be happy to answer any questions. Thank you.