Ambient Ozone Health Effects

Olga Boyko
NJDEP Division of Air Quality

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New York State Department of Health
Topics To Cover

- Ozone Health Effects
- Experimental Studies
  - Human Chamber Studies
- Epidemiological Studies
  - Panel/Field Studies
  - Population-Based Time Series Studies
Ozone Health Effects

- Reactive gas
- Acute effect -- Respiratory irritant
- Chronic effect – Associated with accumulated effects of repeated acute insults (?)
Ozone Health Effects

- Respiratory Effects (lung function, asthma)
- Cardiovascular Effects (arrhythmia, myocardial infarction)
- Daily Mortality (death)
Adapted from: Pryor et al. (1995); Krishna et al. (1998); Bhalia et al. (1999)
History of the Ozone NAAQS

- **1979**: 0.12 ppm for 1 hour
  (revoked in 2005)

- **1997**: 0.08 ppm for 8 hours

- **2008**: 0.075 ppm for 8 hours
Types of Health Studies

- **Experimental study** - laboratory study

- **Epidemiological study** – a statistical study on human populations, which attempts to link human health effects to a specified cause
Ozone Health Studies

Experimental studies
- Human clinical chamber studies
- Animal toxicology studies
- In vitro/mechanistic studies

Epidemiology studies
- Field studies
- Panel studies
- Population studies
Experimental Studies

**Strengths**
- Exposures are controlled
- Almost all sources of variation excluded
- Provides strong evidence of causality
- Prospective studies

**Limitations**
- (Usually) Very high dose
- (Often) Not humans (species-to-species extrapolations required)
- (Usually) Inbred animals
- Restrictive exposure conditions
Epidemiological Studies

Strengths
- No need to extrapolate across species
- Provides direct evidence of human effects

Limitations
- Exposures are complex and always changing
- Exposures are to many chemicals
- Difficult to control for bias and confounding factors (correlation vs. causality)
- Retrospective evaluations
- Conclusions require weight-of-evidence judgments based on entire body of evidence vs. causality criteria
Highlights from a number of Ozone Studies
Human Chamber Studies

- Observed effects at near-ambient concentrations for one to several hours:
  - Spirometry effects (e.g., ↓ FEV1)
  - Bronchoconstriction
  - Airway hyper-responsiveness
  - Lung inflammation
  - Airway cell damage
  - Shallow/rapid breathing pattern
  - Airway irritation – cough/pain on inspiration
Near-Ambient Chamber Data (Adams & McDonnell et al)

- Exposure conditions:
  - ozone or filtered air
  - 6.6 hr total exposure time
  - intermittent exercise (50 min/hr)

- Main conclusions:
  - Significant effects at 0.080 ppm --
    - FEV1 decrement
    - Increased symptom score & PDI
  - No significant group effects at < 0.080 ppm
Near-ambient chamber data

A.

B.
<table>
<thead>
<tr>
<th>Health Effect</th>
<th>Exercise Level</th>
<th>Prolonged Exposure</th>
<th>Short-term Exposure</th>
<th>Lowest Ozone Effect Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Function Decrement</td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td>1 hr</td>
<td>0.06 ppm</td>
</tr>
<tr>
<td></td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td>1-3 hr</td>
<td>0.08 ppm</td>
</tr>
<tr>
<td></td>
<td>Moderate 4.6 hr</td>
<td>4.6 hr</td>
<td>1-3 hr</td>
<td>0.10 ppm</td>
</tr>
<tr>
<td></td>
<td>Moderate 3.0 hr</td>
<td>3.0 hr</td>
<td>1-3 hr</td>
<td>0.12 ppm</td>
</tr>
<tr>
<td></td>
<td>Competitive</td>
<td></td>
<td></td>
<td>0.12-0.14 ppm</td>
</tr>
<tr>
<td></td>
<td>Very Heavy</td>
<td></td>
<td></td>
<td>0.16 ppm</td>
</tr>
<tr>
<td></td>
<td>Heavy</td>
<td></td>
<td></td>
<td>0.18 ppm</td>
</tr>
<tr>
<td></td>
<td>Moderate Light 1.3 hr</td>
<td></td>
<td></td>
<td>0.30 ppm</td>
</tr>
<tr>
<td></td>
<td>At rest</td>
<td></td>
<td></td>
<td>0.37 ppm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50 ppm</td>
</tr>
<tr>
<td>Increased Respiratory Symptoms</td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td>1-3 hr</td>
<td>0.06 ppm</td>
</tr>
<tr>
<td></td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td>1-3 hr</td>
<td>0.08 ppm</td>
</tr>
<tr>
<td></td>
<td>Very Heavy</td>
<td></td>
<td></td>
<td>0.12 ppm</td>
</tr>
<tr>
<td>Airway Responsiveness</td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td>1-3 hr</td>
<td>0.08 ppm</td>
</tr>
<tr>
<td></td>
<td>Very Heavy</td>
<td></td>
<td></td>
<td>0.18 ppm</td>
</tr>
<tr>
<td></td>
<td>At rest</td>
<td></td>
<td></td>
<td>0.40 ppm</td>
</tr>
<tr>
<td>Respiratory Inflammation</td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td>1-3 hr</td>
<td>0.08 ppm</td>
</tr>
<tr>
<td></td>
<td>Very Heavy</td>
<td></td>
<td></td>
<td>0.20 ppm</td>
</tr>
<tr>
<td>Changes in Host Defenses</td>
<td>Moderate 6.6 hr</td>
<td>6.6 hr</td>
<td></td>
<td>0.08 ppm</td>
</tr>
<tr>
<td>Decreased Exercise Performance</td>
<td>Competitive</td>
<td></td>
<td>1 hr</td>
<td>0.18 ppm</td>
</tr>
</tbody>
</table>
Chamber Study Limitations

- At lowest levels, mainly healthy adults
- Only exposed to ozone; not ambient pollutant mix
- Spirometry changes may not be most sensitive indicator of relevant effects
- Small sample sizes limit statistical power
Epidemiological Studies

Common effect estimate metrics:
- Relative risk (RR): >1 ==> increased risk
- % change in risk: >0 ==> increased risk
  [scaled to change (increment) in pollutant level]
- Odds Ratio (OR): >1 ==> increased risk
Field/Panel Studies

- **Field Study** – scientific study in which the subjects are observed without altering the setting or behavior of those under study.

- **Panel Study** – (cohort study) longitudinal study in which a cross section of variables are measured in the same units over time.
Field/Panel Studies

- Repeated observations of lung function and concurrent exposure levels
- Individual-level data on health endpoint and (sometimes) exposure
- Relatively small sample sizes
Respiratory Field/Panel Studies

80’s/90’s camp studies:

- >600 children, mostly healthy, non-asthmatic; multiple measurements per child
- significant ↓ FEV1 with increased ozone
- ozone predominant ambient pollutant associated with health endpoint
- mean levels -- 0.053 - 0.123ppm
- maximum levels - 0.095 -0.245 ppm
Respiratory Field/Panel Studies


- 8 cities
- > 800 asthmatic children
- daily diaries of peak expiratory flow rate (PEF) and asthma symptoms during June - August 1993
- significant ↓ morning PEF with increased ozone
- significant ↑ symptoms with increased ozone
- ozone effect on PEF largely robust in multi-pollutant models
- ozone symptom incidence effect reduced somewhat in multi-pollutant models but trend remains
- max 8-hour 99th %-ile = 0.066 ppm
- significant result remains after removing days > 0.08 ppm
Respiratory Field/Panel Studies

- Adult hikers at Mt. Washington; multi-hour exposures
- Results, all hikers:
  - significant ↓ FEV1 post- vs. pre-hike
  - strength of effect similar after controlling for PM$_{2.5}$ and acidity (P>0.05)
  - max 8-hour 99th %-ile = 0.089 ppm
### Korrick et al results

**Table 7-1c. Cross-day Percent Changes in FEV$_1$ (95% CI) Associated with Acute Ambient O$_3$ Exposures in Adults, Ordered by Size of the Estimate $^a$**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Population/Analysis</th>
<th>N</th>
<th>Cross-day % Change in FEV$_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Korrick et al. (1998)</td>
<td>Hikers with wheeze or asthma (post-pre-hike)</td>
<td>40</td>
<td>-4.47 (-7.65, -1.29)</td>
</tr>
<tr>
<td>2. Korrick et al. (1998)</td>
<td>Hikers who hiked 8-12 hours (post-pre-hike)</td>
<td>265</td>
<td>-2.07 (-3.78, -0.36)</td>
</tr>
<tr>
<td>3. Korrick et al. (1998)</td>
<td>Hikers age 28-37 years (post-pre-hike)</td>
<td>185</td>
<td>-2.01 (-3.42, -0.60)</td>
</tr>
<tr>
<td>4. Korrick et al. (1998)</td>
<td>Hikers who never smoked (post-pre-hike)</td>
<td>405</td>
<td>-1.77 (-3.24, -0.30)</td>
</tr>
<tr>
<td>5. Korrick et al. (1998)</td>
<td>Hikers male (post-pre-hike)</td>
<td>375</td>
<td>-1.65 (-3.12, -0.18)</td>
</tr>
<tr>
<td>6. Korrick et al. (1998)</td>
<td>Hikers age 38-47 years (post-pre-hike)</td>
<td>142</td>
<td>-1.59 (-3.12, -0.06)</td>
</tr>
<tr>
<td>7. Korrick et al. (1998)</td>
<td>All hikers (post-pre-hike)</td>
<td>530</td>
<td>-1.53 (-2.82, -0.24)</td>
</tr>
<tr>
<td>8. Korrick et al. (1998)</td>
<td>All hikers, with PM$_{2.5}$ and acidity in model (post-pre-hike)</td>
<td>530</td>
<td>-1.44 (-3.32, 0.44)</td>
</tr>
<tr>
<td>9. Korrick et al. (1998)</td>
<td>Hikers age 18-27 years (post-pre-hike)</td>
<td>135</td>
<td>-1.29 (-2.88, 0.30)</td>
</tr>
<tr>
<td>11. Korrick et al. (1998)</td>
<td>Hikers age 48-64 years (post-pre-hike)</td>
<td>68</td>
<td>-1.14 (-3.08, 0.80)</td>
</tr>
<tr>
<td>12. Korrick et al. (1998)</td>
<td>Hikers without wheeze or asthma (post-pre-hike)</td>
<td>490</td>
<td>-1.08 (-2.49, 0.33)</td>
</tr>
<tr>
<td>13. Korrick et al. (1998)</td>
<td>Hikers who hiked 2-8 hours (post-pre-hike)</td>
<td>265</td>
<td>-0.99 (-2.70, 0.72)</td>
</tr>
</tbody>
</table>
Population-Based Studies

- Acute endpoints assessed via daily time-series analysis
- Large sample sizes
- Consistent statistical design across studies
- Area/regional monitor exposure data
- More severe endpoints (e.g., hospitalizations)
- Confounding important consideration, e.g.:
  - temperature, season, day of week, co-pollutants, local exposures, socioeconomic status (SES)
Population-Based Studies

- Have looked at relationship between ozone levels and
  - emergency department visits
  - unscheduled hospitalizations
  - mortality (death)
Figure 7.12. Ozone-associated percent change (95% CI) in total respiratory hospitalizations with adjustment for PM indices per standardized increment (see Section 7.1.3.2). Analyses performed using all-year data unless noted otherwise.
Population-based Studies -- summary

% increase in risk per standard increment

- Respiratory Emergency Department Visits
- Respiratory Hospital Admissions
- Respiratory Mortality

- all year
- warm season only

- Asthma
- COPD
- Pneumonia
- Respiratory Infection
Acute Cardiovascular Effects

Panel Studies on Heart Rhythm Variables (ARIC, NAS, HSPH):

- Ozone associated with reduced HRV & ventricular arrhythmias
- PM effects on HRV generally larger and more consistent for different outcome measures
- Ozone effect on arrhythmias robust in two-pollutant models
Acute Cardiovascular Effects

Panel Studies on Myocardial Infarction

- **MONICA:**
  - Current-day ozone associated with acute MI
  - No PM co-pollutant analysis
- Peters et al. (2001):
  - Non-significant trend toward increased risk with increased ozone in previous 2 hours
  - PM effects were stronger
Acute Cardiovascular Effects

Overall Summary:
- Results from field/panel studies are suggestive of an association between ozone and cardiac outcome measures.
- Results from hospitalization time-series studies are inconclusive.
Chronic Respiratory Effects

1996 AQCD:
- Repeated exposure studies in animals show irreversible lung damage
- Human epidemiology data too limited to conclude whether chronic effects occur

More recent longitudinal & retrospective epidemiology studies focus on asthma development & lung-function development
Chronic Respiratory Effects

Seasonal Studies show

- Lung-function growth in children inversely related to summer ozone concentrations
- Limited evidence of recovery in lung-function parameters after ozone season
Chronic Respiratory Effects

Children’s Health Study

- Long-term cohort from 12 SoCal communities
- Cross-sectional analyses:
  - Self-reported asthma prevalence, cough, bronchitis & wheeze unrelated to max 1hr ozone
  - Limited evidence of reduced baseline lung function in females related to annual average ozone
  - Limited evidence of reduced lung function growth related to ozone levels, but weaker than PM$_{10}$ effects (subset who moved from area)
Chronic Respiratory Effects

Children’s Health Study

- Longitudinal analysis (first cohort):
  - Annual average 8hr or 24hr ozone unrelated to lung function growth measures
  - Annual average 8hr or 24hr ozone unrelated to reduced FEV1
  - Significant effects on FEV1 and lung function growth detected for other pollutants
Chronic Respiratory Effects

Development of Asthma

- **Children’s Health Study**
  - No increased risk comparing high ozone to low ozone communities
  - Within high ozone communities RR = 3.3 for those playing 3+ sports vs. no sports
  - No relationship to sports activity in low ozone communities (effect modification)
  - No effects of other pollutants on asthma incidence
Chronic Respiratory Effects

Development of Asthma

- **AHSMOG**
  - 15-year prospective follow up of new-onset asthma in non-smoking white adults
  - Increased risk of asthma in males, but not females
  - No effects of other pollutants on asthma incidence
  - Ozone effect robust to co-pollutants
  - Robust effect in 2 follow-up periods, but limited generalizability
Chronic Respiratory Effects

Retrospective Lung Function Studies

- Yale freshmen
  - Reduce lung function in cohort from high ozone communities vs. low ozone communities
  - Effect stronger in males than females
  - No co-pollutant analysis

- UC Berkley freshmen
  - Reduced lung function comparing student from LA area to students from San Francisco area when adjusting for intrinsic airway diameter
  - Robust effect in multipollutant models
Chronic Respiratory Effects

Summary

- Some suggestive evidence of increased **asthma** incidence & decreased **lung function** growth
- Large prospective cohort study found little relationship to ozone compared to co-pollutants
- Ecological designs harder to control for exposure mis-classification & confounding
- Overall evidence for **chronic respiratory morbidity** inconclusive
Daily Mortality Studies

Population-Based Time Series Studies

Estimating associations between mortality and daily variations in population average exposures
Daily mortality -- single-day lag

% Change in Mortality

U.S. and Canada
- Bell et al. (2004): U.S. 95 communities
- Samet et al. (2008); reanalysis Dominici et al. (2003): U.S. 90 cities
- Schwarz (2003): U.S. 14 cities
- Kinney and Özlüyak (1991): Los Angeles County, CA
- Kinney et al. (1995): Los Angeles County, CA
- Fairley (2003): Santa Clara County, CA
- Dockery et al. (1992): St. Louis, MO
- Lippmann et al. (2000); reanalysis: Houston, TX
- Chock et al. (2000): Pittsburgh, PA (age 0-74)
- Dockery et al. (1992): Eastern Tennessee
- Villeneuve et al. (2003): Vancouver, Canada (age 65+)

Europe
- Prescott et al. (1998): Edinburgh, Scotland
- Zmirou et al. (1996): Lyon, France
- Hoek et al. (2000); reanalysis: Hoek, 2003: The Netherlands
- Roemer and van Wijnen (2001): Amsterdam, the Netherlands
- Verheijen et al. (1996): Amsterdam, the Netherlands
- Peters et al. (2000a): Coal basin in Czech Republic
- Peters et al. (2000b): NE Bavaria, Germany
- Garcia-Aymerich et al. (2000): Barcelona, Spain
- Suyer et al. (1996): Barcelona, Spain

Latin America
- Borja-Aburto et al. (1997): Mexico City
- Borja-Aburto et al. (1998): SW Mexico City
- Gouveia and Fletcher (2000b): São Paulo, Brazil
- Ostro et al. (1996): Santiago, Chile

Australia
- Morgan et al. (1998b): Sydney, Australia
- Simpson et al. (1997): Brisbane, Australia

Asia
- Kim et al. (2004): Seoul, Korea
- Lee et al. (1999): Seoul, Korea
- Lee and Schwartz (1999): Seoul, Korea
- Lee et al. (1998): Ulsan, Korea

Best of lag 0 to 3 by city
- lag 0
- lag 1
- lag 1
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 0
- lag 1
Daily mortality -- multi-day lag

% Change in Mortality

U.S. and Canada

- Bell et al. (2004): U.S. 95 communities
- Gamble (1998): Dallas, TX
- Ito and Thurston (1996): Cook County, IL
- Lippmann et al. (2000): Reanalysis Ito, 2004: Detroit, MI
- Lipfert et al. (2000a): 7 counties in PA and NJ
- Klemm et al. (2004): Atlanta, GA (age 65+)
- Villeneuve et al. (2003): Vancouver, Canada (age 65+)

Europe

- Gryparis et al. (2004): 23 European cities
- Hoek et al. (2000; reanalysis Hoek, 2003): The Netherlands
- Roemer and van Wijnen (2001): Amsterdam, the Netherlands

Latin America

- Borja-Abruto et al. (1998): SW Mexico City
- O’Neill et al. (2004): Mexico City

Multicity combined

- Lag 0-8
- Lag 1-2
- Lag 0-1
- Lag 0-3
- Lag 0-1
- Lag 0-2
- Lag 0-1
- Lag 0-6
- Lag 1-2
- Lag 0-1

SE not given; significant at $p = 0.065$
Bell et al/NMMAPS: 24-hour ozone 90th %-ile values range from ~0.025 - 0.060 ppm

Pooled effect estimate robust to:

PM excluding high temperature days excluding high ozone days (> 0.060 ppm 24-hour average ozone)
Daily mortality -- meta-analysis summary

- Bell et al. (2005): 32 U.S. and non-U.S. studies (41 estimates)
- Ito et al. (2005): 38 U.S. and non-U.S. studies (43 estimates)
- Levy et al. (2001): 6 U.S. and European studies (6 estimates, PM-adjusted)
- Levy et al. (2005): 28 U.S., Canadian, and European studies (48 estimates)
- Stieb et al. (2003): 10 U.S. and non-U.S. studies (10 estimates, non-GAM studies only)
- Thurston and Ito (2001): 7 U.S. and European studies (7 estimates, PM-adjusted)
- World Health Organization (2004): 8 European studies (15 estimates)
Daily Mortality

Summary

- Robust association between daily mortality and increased ozone
- Not sensitive to co-pollutants, daily weather
- Larger risks in analyses limited to warm season
- Cardiovascular mortality somewhat stronger and more consistent than respiratory
1996 Ozone EPA AQCD*

Most conclusive evidence:
- Controlled acute human exposures
  - Acute lung function deficits (e.g., reduced FEV1)
- Field/panel studies
  - Acute lung function deficits (e.g., reduced PEF)

Highly suggestive evidence:
- Associations w/ respiratory emergency department (ED) visits, hospitalizations
- Co-pollutant interactions & chronic effects unclear

*AQCD = Air Quality Criteria Document
Further evidence from controlled exposures
- Suggestion of sensitive individuals below 0.08 ppm

Much larger epidemiology database:
- Acute respiratory effects considered causal
- Strong evidence of association w/daily mortality
- Cardiovascular effects suggestive, but evidence inconclusive
- Chronic respiratory effects inconclusive
- Lack of conclusive evidence for several other endpoints (chronic mortality, lung cancer, developmental effects)