Air Pollution and Health

Chapter 5-Health Effects
Modified for EOH 468
Spring 2008

Air pollution episodes

• Short-term increases in pollutant concentrations above normal levels
• Vary in intensity
Air pollution episodes

• Notable episodes include
  – Meuse Valley, Belgium, 1930
  – Donora, Pa., 1948
  – London 1952, 1956

Air pollution episodes

• Extreme episodes result in illness and death
• Studies of minor episodes shows significant associations between elevated pollutant levels, acute illness, and even increased death rates
Pollutant exposures & cause-effect relationships

• Pollutants and acute effects
  – Eye, nose, throat irritation
  – Asthmatic attacks
  – Premature death

Pollutants and chronic exposures

• Chronic effects
  – Major focus of air pollution regulation
    • Respiratory and cardiovascular disease
    • Neurotoxic effects
    • Cancer
Cause-effect relationships

• Must be reasonably established to regulate pollutants
• Establishing causation is a difficult undertaking
• Convergence of evidence from epidemiological, toxicological, and occupational exposure studies

Epidemiological studies

• Used to determine potential relationships between environmental factors and disease
• Application of statistical analyses of data collected on health status of study populations, pollutant exposures, and confounding factors
Epidemiological studies

• Designs
  – Cross-sectional
  – Longitudinal
  – Case control
  – Prospective
  – Retrospective

Epidemiological studies

• Increasingly more powerful in showing relationships between pollutants exposures and health effects
• Recent studies are characterized by strong study design, good exposure & health effects data, and large study populations
Confounding factors

• Factors that make it more difficult to identify significant pollutant/health effect relationships
• Include individual sensitivity, age, existing disease, gender, race, socio-economic status, tobacco smoking, lifestyle, occupation, weather, interaction effects

Interaction effects

• Confounding may result due to interactions between
  – Two or more pollutants
  – Pollutants and meteorological variables
  – Pollutants and other exposures
Interactions with other pollutant exposures

- Tobacco smoking may mask health effects associated with pollutant exposures
  - May increase risk by interfering with respiratory clearance mechanisms

Effects of pollutant exposures

Figure 5.1 Prevalence of chronic bronchitis associated with tobacco smoking and exposure to ambient air pollution. (From Lambert, P.M. and Field, D.G., Lancet, 5, 855, 1970. With permission.)
Exposure assessment

- Place of residence
- Personal exposure monitors
- Fixed site monitors
- Dispersion modeling

Population susceptibility

- Variations in individual sensitivity/susceptibility complicate epidemiological assessments
Population susceptibility

- Identifying populations at risk
  - Very young, aged
  - Individuals with existing respiratory or cardiovascular disease
  - Individuals occupationally exposed
  - Smokers

The case for causation

- High probability of disease association
  - Number of different populations in with similar association is observed
    - Different population groups, climate, times of year
    - Increasing severity with increasing exposure
    - Biologically plausible mechanism
Pollutant effects on humans

- Effects on specific target organs
  - Direct
  - Indirect

Target organs

Figure 5.2 Target organs for air pollutant exposures.
Eye irritation

• One of the more common effects of pollutant exposures
• Common ambient irritants include
  – Acrolein
  – Formaldehyde
  – PAN

Cardiovascular system effects

• Primary pollutant concerns include
  – Carbon monoxide
  – Lead
  – Fine particles
Cardiovascular system effects

- Carbon monoxide binds to hemoglobin which reduces oxygen transport to vital tissues
- Lead interferes with formation of hemoglobin

Cardiovascular system effects

- Individuals with severe chronic respiratory disease often die of cor pulmonale (heart failure)
- Premature cardiovascular system related mortality strongly associated with exposures to PM$_{2.5}$
Respiratory system

- Function is to supply body with oxygen
- Directly exposed to toxic pollutants
- Pollutant effects determined by structural anatomy

Respiratory defense mechanisms

- Nasal hairs-filter large particles
- Nasal passages-impaction on mucus secreting surfaces, removal by cilia
- Cough/sneeze reflex
- Tracheal-bronchial, mucus-cilia escalator
- Phagocytes in pulmonary region
Pollutants and respiratory disease

- Exposure may cause/contribute to
  - Chronic bronchitis
  - Pulmonary emphysema
  - Lung cancer
  - Bronchial asthma
  - Infections

Chronic bronchitis

- Characterized by inflammation of the membranes of the respiratory airways
- Caused by extended mucous membrane irritation
Chronic bronchitis

• Symptoms include
  – Persistent cough
  – Excessive sputum production

Chronic bronchitis

• Commonly accompanied by
  – Destruction of cilia, membrane thickening
  – Swelling of inflammed membranes
  – Increased airway resistance-difficulty in breathing
  – Part of COPD/COLD syndrome
Chronic bronchitis

- Exposure to tobacco smoke is the most common cause
- Suggestive evidence that exposure to $\text{SO}_2$ and PM may contribute to chronic bronchitis

Pulmonary emphysema

- Disease of lung tissue
- Common in older adults
- Characterized by degeneration of alveolar tissue
  - Reduces surface area available for gas exchange
Pulmonary emphysema

- Adverse effects include
  - Pulmonary hypertension
  - Shortness of breath
  - Difficulty exhaling

Lung cancer

- Leading cause of cancer deaths in the U.S.
- Typically a disease of individuals in late middle-age and beyond
- Most common form is bronchiogenic
Lung cancer

- Major causes include exposures to
  - Tobacco smoke
  - Asbestos
  - Arsenic
  - Radioactive isotopes

Lung cancer

- Relationships to ambient pollutant exposures
  - Lung cancer rates are higher in urban areas
  - Lung cancer rates are higher in migrants from high pollution to low pollution countries
Lung cancer

• Relationships to ambient pollutant exposures
  – Cancer rates and air pollution indices
    • 8 % increase in lung cancer mortality for every 10 µg/m³ increase in PM$_{2.5}$

Asthma

• Acute respiratory ailment
  – Characterized by episodic constriction of airway muscles, excessive mucus production, and increased airflow resistance
Asthma

• Acute respiratory ailment
  – Symptoms
    • Severe shortness of breath
    • Wheeze
    • Chest tightness
    • Cough

Asthma

• Prevalence in U.S. - 4.3 %
• Prevalence in U.S. children
  – 8.3 % in Midwest
  – 7.8 % in the South
  – 13.4 % in African-Americans
Asthma

- Linked with exposure to allergens
- Air pollutants may potentiate allergenic responses that cause asthma
- Asthmatic attacks caused by exposure to
  - Inhalant allergens
  - Nonspecific gas/particulate phase substances

Asthma

- Sulfur dioxide exposures have been shown to induce asthmatic attacks under controlled exposure studies
- Ozone exposures linked to emergency room visits by children
- Ambient $O_3$ exposures may also contribute to asthma development
Respiratory system infections

• Animal studies
  – Pollutant exposures increased risk of respiratory system infections
    • Ozone, NO\textsubscript{2}, SO\textsubscript{2}, and PM

Respiratory system infections

• Human exposure studies/epidemiological studies
  – Young and aged have a greater risk of infection
Health effects of regulated pollutants

- Criteria pollutants
- Hazardous air pollutants

Criteria pollutants

- Carbon monoxide
- Sulfur oxides
- Particulate matter
- Hydrocarbons
- Nitrogen oxides
- Ozone
- Lead
Carbon monoxide

• Lethal at high concentrations (> 1000 ppmv)
• Sub-lethal symptoms (several hundred ppmv)
  – Headache, fatigue
  – Nausea, vomiting

Carbon monoxide

• Such health effects associated with
  – Poorly vented combustion appliances
  – Idling motor vehicles
  – Occupational industrial activities
  – Smoke inhalation from structural fires
Carbon monoxide

- Ambient exposures typically less than those that cause acute effects
- Binds with hemoglobin reducing the blood’s ability to transport $O_2$
  - Forms carboxyhemoglobin

Carbon monoxide

- Carboxyhemoglobin formation is a direct function of exposure concentration and duration

![Graph of COHb levels in the blood as a function of exposure concentration, duration, and ventilation rate. (From USEPA, 27F000608-000413-EP, Washington, D.C., 1993.)]
Carbon monoxide

• Primary health concerns
  – Effects on
    • Cardiovascular system
    • Neurobehavioral

Carbon monoxide

• Cardiovascular system effects
  – Patients with angina experienced exercise-induced ischemia (O₂ deficiency at carboxyhemoglobin levels of 3 to 4 %)
  – Confounded by cigarette smoking which is a major source of CO exposure
Carbon monoxide

• Cardiovascular system effects
  – Chronic exposures may cause atherosclerosis
  – Acute exposures may trigger arrhythmias and myocardial infarction

Carbon monoxide

• Neurobehavioral affects
  – Caused by reduced $O_2$ and the brain
  – Reduced hand to eye coordination, vigilance, continuous performance
Carbon monoxide

• Response to COHb levels

<table>
<thead>
<tr>
<th>Blood COHb (%)</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>None known</td>
</tr>
<tr>
<td>2.0</td>
<td>Quicker onset of angina pain in exercising patients; pain duration lengthened</td>
</tr>
<tr>
<td>2.5</td>
<td>Impairment of time interval discrimination</td>
</tr>
<tr>
<td>3.0</td>
<td>Change in relative brightness thresholds</td>
</tr>
<tr>
<td>4.5</td>
<td>Increased reaction time to visual stimuli</td>
</tr>
<tr>
<td>10–20</td>
<td>Performance changes in driving simulation</td>
</tr>
<tr>
<td>10–20</td>
<td>Headache, fatigue, dizziness, coordination loss</td>
</tr>
</tbody>
</table>


Sulfur oxides

• Sulfur dioxide
• Particulate-phase $\text{SO}_x$
  – Acid sulfate
Sulfur dioxide

- Information on acute/chronic effects based on laboratory exposure studies
- Highly soluble in tissue fluids
  - Removed in upper respiratory tract
  - Forms sulfurous acid

Sulfur dioxide

- Major physiological effects
  - Changes in mechanical function of upper airways
    - Increasing nasal flow resistance
    - Decrease in mucous flow rate
Sulfur dioxide

• Major physiological effects
  – Affect pulmonary defense mechanisms such as mucociliary transport, alveolar clearance of particles, macrophage function

Sulfur dioxide

• Major health effects
  – Limited evidence to indicate that exposures may cause chronic bronchitis
  – Bronchoconstriction, decreased expiratory flow rates, clinical symptoms of shortness of breath and wheezing in asthmatics
Sulfur dioxide

• Effects on asthmatics
  – Initiated at exposures of 0.25-0.30 ppm for 5 and-10 minutes
  – Mild-moderately asthmatic children and adults are at greatest risk during exercise

Acid sulfate

• Sulfuric acid is a strong irritant
• Consistent effects on respiratory function in adults has not been shown
• Asthmatics may be more sensitive
Acid sulfate

- Can affect pulmonary defense mechanisms
- Biological responses may be due to the deposition of $\text{H}^+$

Acid sulfate

- Few epidemiological studies conducted that have measured acid aerosols
- Acid aerosols have been related to significantly higher prevalence of bronchitis in children, reduced lung function
Particulate matter

• Particles must enter and be deposited in respiratory tract
  – Depends on aerodynamic size, respiratory defense mechanisms, and breathing pattern

• Describes inhalable (IPM), thoracic (TPM) and respirable (RPM) particles

Particulate matter

• Particle penetration into respiratory system
Particulate matter

• Inhalable-enters upper airway of the head
• Thoracic-enters airways and gas exchange region of lung, significant public health concern
• Respirable-high probability of being deposited in respiratory system, significant public health concern

Particulate matter

• Respiratory deposition
  – Function of aerodynamic diameter
  – Occurs by impaction, sedimentation, diffusion
  – Site of deposition determines mechanisms and rate of clearance, potential for retention and dissolution, and location and nature of tissue injury
Particulate matter

• Fractional deposition efficiency

![Graph showing deposition efficiency for different particle sizes.](image)

Figure 5.4 Deposition of particles of varying size in nasopharyngeal, tracheobronchial, and pulmonary regions of the lung. (From Pizer, S.M. Jr., Air Pollution and Health, Hogaboam, S.C., Burner, J.M., Kozel, H.S., and Malm, R.L., Eds., Academic Press, San Diego, 1989, p. 394. With permission.)

Particulate matter

• Deposition affected by
  – Mass concentrations
  – Molecular composition
  – pH
  – Solubility
Particulate matter

• Deposition varies among smokers, nonsmokers, individuals with lung disease
  – Increased deposition in individuals with lung disease

Particulate matter

• Particle retention
  – Depends on clearance rates

• Clearance rates
  – Vary among different regions
    • Nose and upper airways-less than one day
    • Alveoli -weeks to months
  – Slow clearance more harmful
Particulate matter

• Studies in 1980s and 1990s observed significant associations between particulate matter levels and adverse health effects
  – Respiratory hospitalizations
  – Lung function changes
  – Respiratory symptoms
  – School absenteeism
  – Premature mortality

Particulate Matter

• The next set of slides, on the health effects of exposure to particulate matter come from a presentation by C. Arden Pope III and Douglas W. Dockery.

• For our class, we need to understand that the connection between exposure to fine particulates (PM$_{2.5}$) and health is complex, but regulatory action is moving forward.

• Video on children’s health and Air Pollution: http://www.aqmd.gov/pubinfo/video/childeng.htm
Short-term exposure and mortality

1930s-mid 1980s.
- Episode and misc. studies.

Late 1980s-1990s.
- Early formal daily-time series studies reported and replicated.
- Use of increasingly rigorous time-series modeling techniques
- Explosion of single-city studies

1997-2006
- Continued development of time-series modeling
- Use and further development of the case-crossover design
- Meta analyses
- Multi-city daily time-series and case-crossover studies

10 μg/m³ PM$_{2.5}$ or 20 μg/m³ PM$_{10}$ → 0.4% to 1.5% increase in relative risk of mortality—Small but remarkably consistent across meta-analyses and multi-city studies.

Table 1. Comparison of percent estimated percentage increase (95% confidence or posterior interval, CI, or t value) in relative risk of mortality estimated across meta-analyses and multi-city studies of short-term (6 h) changes in exposure.

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary Sources</th>
<th>Exposure Increment</th>
<th>All Cause</th>
<th>Cardiovascular</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analyses of 24 studies</td>
<td>Levy et al. 2003</td>
<td>20 μg/m³ PM$_{2.5}$</td>
<td>1.5 (1.2, 1.7)$^a$</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Meta-analyses: SAM-based studies</td>
<td>Stieb et al. 2002, 2009$^{3,4,6}$</td>
<td>20 μg/m³ PM$_{2.5}$</td>
<td>1.4 (1.2, 1.6)$^b$</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Non SAM-based studies</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Meta-analyses from single-city studies</td>
<td>Anderson et al. 2008$^{7,8}$</td>
<td>20 μg/m³ PM$_{2.5}$</td>
<td>1.2 (0.9, 1.6)$^c$</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Meta-analyses from CVMAP report to the U.K. Department of Health on Cardiovascular Disease and Air Pollution (12+ studies, 170+ cities)</td>
<td>–</td>
<td>–</td>
<td>1.0 (0.7, 1.3)$^d$</td>
<td>1.8 (0.4, 3.6)$^e$</td>
<td>–</td>
</tr>
</tbody>
</table>

*Includes: SAM-based analyses with potentially inadequate convergence, ischemic heart disease deaths; *Chronic obstructive pulmonary disease deaths; *Cardiovascular and respiratory deaths combined.
Long-term exposure and mortality

1970s-
• Population-based cross-sectional studies reported associations between long-term average fine PM and mortality rates.
• These studies discounted—couldn’t control for smoking and other individual risk factors.

1993, 1995
• Harvard Six-Cities and ACS Prospective Cohort studies were reported.
• Long-term fine PM exposure was associated with mortality even after controlling for cigarette smoking and other individual risk factors.

1997-2006
- HEI reanalyzes Six-cities and ACS studies
- Other extended analyses of Six-Cities & ACS
- Several other independent studies reported.
- http://www.healtheffects.org/Pubs/st-reanalysis.htm for summary

10 μg/m³ PM$_{2.5}$ → approximately 6% to 17% increase in relative risk of mortality, with some outliers.

Generally bigger effects on cardiopulmonary/cardiovascular disease mortality.
Time scales of exposure--issues

- Are the excess deaths observed in the short-term studies due primarily to mortality displacement (harvesting)?

- Why are the PM-mortality effect estimates from the long-term studies so much larger than from the short-term studies?

- Can we learn more about the dynamic exposure-response relationship by integrating evidence from long-term, intermediate, and short-term time scales?
Figure 1. Comparison of % change in risk of mortality associated with an increment of 10 μg/m³ PM_{2.5} or 20 μg/m³ PM_{10} or BS estimated for different time scales of exposure (approximate number of days, log scale).

**Time scales of exposure--conclusions**

- Short-term studies are observing more than just harvesting or mortality displacement:
  --little short-term compensatory reduction in deaths
  --larger effects for intermediate and longer-term time scales.

- Adverse health effects are dependent on both exposure concentrations and length of exposure.

- Long-term exposures have larger more persistent cumulative effects than short-term exposures.
Shape of concentration-response (C-R) function--
outline

1984, 1990
• Early analyses of concentration-response function.
• Used London mortality data for 14 winters
• C-R function less steep at higher concentrations
• No evidence of a threshold

Early to Mid 1990s
• Many single-city time series studies used quintile
  (or quartile) analysis, spline functions, or non-parametric
  smoothing that allowed for flexible fitting C-R function.
• C-R were generally (but not always) near linear with no
  clear threshold.

1997-2006
➢ Combined or “meta-smoothed” C-R function estimated using multiple
cities—enhancing statistical power and generalizability.
➢ Extended analyses of C-R function in prospective cohort and related
  studies.

Figure 1. Selected concentration-response relationships estimated from various multi-city
daily time-series studies (approximate adaptations from original publications rescaled for comparison
purposes).
Cardiovascular disease--outline

1930s-1950s
- Excess deaths in early severe air pollution episodes were due to both respiratory and cardiovascular disorders, often in combination.

Early to Mid 1990s
- Much of the research focused on respiratory disease, but—
- Daily time series studies observed PM associations with deaths and hospitalizations for both respiratory and cardiovascular disease.
- PM was strongly associated with cardiopulmonary mortality in the early prospective cohort studies.

1997-2006
- Dramatic growth in studies of air pollutions and cardiovascular disease.
- Studies of air pollution and cardiovascular disease being published and discussed in the cardiovascular journals.
Outline of cardiovascular and related effects

**Long-term PM exposure**
- Cardiovascular mortality
- Blood markers of cardiovascular risk (fibrinogen, platelets, white blood cells)
- Histopathologic markers of sub-clinical chronic inflammatory lung injury
- Subclinical atherosclerosis (carotid intima-media thickness, CIMT)

**Short-term PM exposure**
- Cardiovascular mortality
- Cardiovascular hospital admissions
- Stroke mortality and hospital admissions
- MI
- Hypoxemia (S_{O2})
- HR and HRV
- Various markers of inflammation
- Cardiac arrhythmia/cardiac arrest/sudden cardiac death
- ST-segment depression and cardiac repolarization
- Blood pressure/arterial vasoconstriction/vascular reactivity and endothelial function

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**Figure 3.** RR for CV mortality associated with a 10-μg/m³ in long-term PM_{2.5}.
Biological Plausibility

1997

The 1997 Critical Review noted that:
"Weak biological plausibility has been the single largest stumbling block to accepting the association as causal. There is no known mechanism whereby exposure to very low concentrations of inhaled particles would produce such severe outcomes as death, even from respiratory disease, and certainly not from cardiovascular disease."

1997-2006

"It is no longer true that there are no known mechanisms or plausible pathophysiological pathways"

Biological Plausibility—Case study of biological effects of exposure to Oil Fly Ash (Ghio et al. 1999)

Case:
• 42-yr-old, never smoker, male, diabetic
• Exposed to aerosolized oil fly ash particles due to cleaning oil-burning stove in home

Within 24 hrs developed:
• Shortness of breath
• Nonproductive cough
• Wheezing

Over weeks:
• Hypoxic respiratory failure
• Abnormal blood indices
• Particle laden macrophages
• Diffuse alveolar damage
• Angina

Evidence that PM-cardiorespiratory effects are biologically plausible?
### Biological Plausibility–Utah Valley PM

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<tbody>
<tr>
<td>• Increased pediatric respiratory hospital admissions</td>
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<td>• Increased respiratory symptoms</td>
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<td>• Reduced lung function</td>
<td></td>
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<tr>
<td>• Increased school absences</td>
<td></td>
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<tr>
<td>• Increased respiratory and cardiovascular deaths</td>
<td></td>
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<tr>
<td>• Acute airway injury and inflammation in rats and humans</td>
<td></td>
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<tr>
<td>• <em>In vitro</em> oxidative stress and release of proinflammatory mediators by cultured respiratory epithelial cells</td>
<td></td>
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<tr>
<td>• Differential toxicities of PM when the mill was operating versus when it was not (metals content and mixtures?)</td>
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#### Evidence of biologically plausibility?

### Biological Plausibility–Hypothesized general pathophysiological or mechanistic pathways

Much recent research has focused on four interrelated general pathophysiological pathways:

1. **Accelerated Progression and exacerbation of COPD**

2. **Pulmonary/Systemic Oxidative Stress, Inflammation, Accelerated Atherosclerosis**

3. **Altered Cardiac Autonomic Function**

4. **Vasculature alterations**
Accelerated Progression and exacerbation of COPD

Long-term PM exposure associated with:

- Pulmonary retention of fine PM and small airway remodeling contributing to COPD (Brauer et al. 2001; Churg et al. 2003)
- Deficits in lung function (Ackermann-Liebrich et al. 1997)
- Increased symptoms of obstructive airway disease (chronic cough, bronchitis, chest illness)
- Deficits in rate of lung function growth in children (Gauderman et al. 2004)

Short-term PM exposure associated with:

- Exacerbations of respiratory symptoms
- Transient declines in lung function
- Aggravate background inflammation in COPD (MacNee and Donaldson 2000, 2003)

COPD, indicated either by symptoms or deficits in FEV₁, is a substantial risk factor for CVD (van Eeden et al. 2005; Sin et al. 2005)

Pulmonary/Systemic Oxidative Stress/Inflammation and Accelerated Atherosclerosis

- Inflammation (and blood lipids) contribute to the initiation and progression of atherosclerosis.
- Long-term PM exposure → low to moderate grade inflammation → initiate and accelerate atherosclerosis.
- Short-term PM exposures and related inflammation may contribute to acute thrombotic complications of atherosclerosis increasing the risk of making atherosclerotic plaques more vulnerable to:
  - rupture
  - clotting, and
  - precipitating acute cardiovascular or cerebrovascular events (MI or ischemic stroke).
Inflammation/Accelerated Atherosclerosis is supported by evidence that:

**Long-term PM exposure associated with:**
- Blood markers of cardiovascular risk (fibrinogen levels, counts of platelets and WBCs) (Schwartz 2001)
- Subclinical chronic inflammatory lung injury (Souza et al. 1998)
- Subclinical atherosclerosis (carotid intima-media thickness, CIMT) (Kunzli et al. 2005)

**Short-term PM exposure associated with:**
- CRP/other markers of inflammation and oxidative stress (Table 4 in Crit. Rev.)
- Ischemic stroke events (Wellenius et al. 2005; Dominici et al. 2006)
- ST-segment depression (Pekkanen et al. 2002; Gold et al. 2005)
- Myocardial ischemia (in dogs) Wellenius et al. 2003)

A series of studies by van Eeden, Hogg, Suwa et al. (1997-2002) suggest:

- PM exposure
  - Pulmonary inflammation
  - Systemic inflammatory responses (including release of inflammatory mediators, bone marrow stimulation and release of leukocytes and platelets)
  - Progression and destabilization of atherosclerotic plaques

In rabbits naturally prone to develop atherosclerosis they found that:

- PM exposure
  - Accelerated progression of atherosclerotic plaques with greater vulnerability to plaque rupture
Altered Cardiac Autonomic Function

In addition to HR and HRV, PM associated with:

- Cardiac Arrhythmia (based on ICD records)  

- Cardiac repolarization  
  (Henneberger et al. 2005)

- Changes in cardiac rhythm or function in animal models  
  (Godleski et al. 2000; Watkinson et al. 2001; Wellenius et al. 2002; Wichers et al. 2004)

In addition to

- Accelerated Progression and exacerbation of COPD
- Pulmonary/Systemic Oxidative Stress Inflammation/Accelerated Atherosclerosis
- Altered Cardiac Autonomic Function
- Vasculature alterations

Other mechanistic pathways include:

- Translocation of particles
- Modulated host defenses and immunity
- Hypoxemia

It is unlikely that any single pathway is responsible.
Gaps in Knowledge--Susceptibility

Various characteristics have been shown to influence susceptibility including:

- Preexisting respiratory or cardiovascular disease
- Diabetes
- Medication use
- Age, Gender, Race
- Socioeconomic status
- Health care availability
- Educational attainment
- Housing characteristics
- Outdoor activity
- Genetic differences

We still need a better understanding of who’s most at risk or susceptible.
Gaps in Knowledge—Infant/Birth Outcomes

There is substantial evidence that PM exposure in children is associated with:
• Deficits in lung function and lung function growth
• Respiratory illness and symptoms
• Respiratory hospitalization

Also evidence that PM exposure increases the risk of
• Infant mortality—especially postneonatal respiratory mortality

There remain serious gaps regarding potential effects on
• Fetal growth
• Premature birth
• Related birth outcomes

Gaps in Knowledge—Lung Cancer

Available evidence suggests small PM-related increased lung cancer risk

but,

Substantial uncertainty remains. . .
Gaps in Knowledge—Relative toxicity and role of sources and copollutants

- Little evidence that a single source or component of PM is solely responsible for health effects, but the relative importance of:
  - particle size
  - secondary inorganic PM
  - solubility
  - metal content
  - surface area and reactivity
  - and other characteristics

- Further study is also needed to understand the relative importance of various sources and related copollutants.

Keep up to date

- Many resources are available to keep up to date (in addition to the technical literature).
- CARB Chairs seminars: [http://www.arb.ca.gov/research/seminars/seminars.htm](http://www.arb.ca.gov/research/seminars/seminars.htm)
Hydrocarbons

• Air quality standards for NMHCs promulgated to achieve O$_3$ standards
• No significant health risks from NMHC exposures

Hydrocarbons

• Aldehydes such as formaldehyde and acrolein are potent mucous membrane irritants
• Polycyclic aromatic hydrocarbons are carcinogenic
• Many are regulated as toxic pollutants
Nitrogen oxides

• Nitrogen dioxide primary health concern
• Animal exposure studies suggest that exposures may contribute to development of emphysema

Nitrogen dioxide

• Epidemiological studies of schoolchildren
  – Decreased lung function
  – Increases in respiratory symptoms with increased exposure concentration
Nitrogen dioxide

- Epidemiological studies of schoolchildren
  - More frequent hospitalizations
  - More treatments for lower respiratory system illness
  - Chronic cough and respiratory system infections with increased annual exposure levels

Nitrogen dioxide

- Studies of potential indoor exposures
  - Gas cooking stoves
    - 20% increase in respiratory illness associated with the presence of gas cooking stove
    - Australian studies reported an increase in asthma by threefold, and respiratory illness by twofold
Ozone

• Variety of physiological/pathological effects in laboratory animal exposures
  – Injury to respiratory airways and alveolar cells
  – Significant lung function changes
    • Increased respiratory rates, pulmonary resistance, etc.

Ozone

• Effects that impair the body’s ability to protect itself from infection
  – Interference with muco-ciliary transport
  – Impaired killing of bacteria
  – Impaired macrophage function

• Mutagenic, genotoxic-has some potential to cause cancer
Ozone epidemiological studies

• Association between daily $O_3$ levels and
  – Decreases in pulmonary function
  – Aggravation of asthma
  – Increases in daily hospital admission
  – Hospital admissions for respiratory illness
  – Premature mortality

Potential reduced health effects

• Compliance with revised $O_3$ standard

Figure 5.9 Estimates of adverse health effects avoided in New York City as a consequence of compliance with the 80 ppbv, 8-hr, NAAQs (from Thurston, G.D. and its, K., in Air Pollution and Health, Holgate, S.T., Samet, J.M., Koren, H.S., and Maynard, R.L., Eds., Academic Press, San Diego, 1999, p. 504. With permission.)
Lead

• Historical exposures
  – Ingestion of liquids stored in lead containers and food from lead soldered cans
  – Lead paint and dusts
  – Airborne lead dust from automobiles
  – Smelter emissions

Lead

• Health effects
  – Target organs
    • Blood
    • Brain
    • Nervous system
    • Kidneys
    • Reproductive system
Lead

• Acute exposures (> 60 µg/dL)
  – Colic
  – Shock
  – Severe anemia
  – Kidney damage
  – Brain-damage
  – Death

• Chronic exposures—variety of symptoms
Lead-health effects

- Related to blood levels
  - Measure of relatively recent exposures
- Very young children a special risk
  - Mental retardation from acute exposures
  - Decreasing cognitive performance from chronic exposures

Lead-health effects

- Levels of concern
- ≥ 10 µg/dl in children
- May result in increased blood pressure in adults at levels < 10 µg/dl
Hazardous air pollutants

• 189 substances are regulated
• Two categories
  – Those regulated prior to 1990
    • Mercury, asbestos, beryllium, vinyl chloride, benzene, arsenic, radionuclides
  – Those identified in 1990 Clean Air Act amendments

Personal air pollution

• Tobacco smoking
  – 40 million Americans
  – 500,000 deaths per year
    • 130,000 deaths due to lung cancer
    • 300,000 deaths due to cardiovascular disease
  – Single most important environmental factor contributing to premature mortality
Personal air pollution

- Tobacco smoke much greater public health problem than ambient air pollution
- Tobacco smoking not regulated—voluntary risk
- Ambient air pollution regulated—involuntary risk