About the Cover
The cover depicts an important episode in aerosol history—the Pasadena experiment and ACHEX. It includes a photograph of three of the key organizers and an illustration of a major concept of atmospheric aerosol particle size distribution. The photograph is from Chapter 8, Figure 1. The front row shows Kenneth Whitby, George Hidy, Sheldon Friedlander, and Peter Mueller; the back row shows Dale Lundgren and Josef Pich. The background figure is from Chapter 9, Figure 13, illustrating the trimodal atmospheric aerosol volume size distribution. This concept has been the basis of atmospheric aerosol research and regulation since the late 1970s.
Introduction

The interface between particles in the air and the human respiratory system has been a subject of inquiry at New York University’s Institute of Environmental Medicine (NYU-IEM) since the establishment of the department in 1954. The original program at NYU emerged in 1947 from the concept that a medical school should be concerned with the health problems of workers and the health risks posed by the environment. A primary interest was in the consequences of exposure to “dusts.” NYU School of Medicine formed a Division of Industrial Medicine and an accompanying institute within the Department of Preventive Medicine, both under the direction of Dr. Anthony Lanza. The department became independent in 1954, with Dr. Norton Nelson as director of both the department and the institute. He served until 1979; during that time, the institute underwent a name change to the Institute of Environmental Medicine in 1967 to reflect the broader scope of research activities then in progress (Nelson, personal communication, n.d.). Later directors of the institute include Drs. Arthur C. Upton (1979–1992) and Max Costa (1993–present).

Researchers were initially interested in the journey that airborne particles make into the human respiratory system. They wanted to learn how likely it is that an inhaled particle will deposit in the lung, where specific particles deposit in the respiratory tract, how rapidly they are cleared, what happens to the retained particles, and how they affect their host. These initial studies of particle inhalation led to investigations of many other aspects of inhalation exposure. Aerosol research expanded to include toxicological studies in vivo and in vitro, field studies of exposure, epidemiological investigations of human response to inhaled particles, and current studies on genetic
susceptibility to components of airborne particulate matter (PM). An important goal of the research was, and is, to develop information that could lead to interventions that will prevent harm to cardiopulmonary and general health.

**Particles in the Lung**

NYU-IEM has a rich history of research on the deposition and fate of inhaled particles in the lung. Studies have included detailed measurement of monodisperse particle deposition in humans, animals, and airway cast models.

In a 1986 paper on the use of airborne particles to measure air flow, function, and clearance in the respiratory system, Dr. Nelson noted that in the preceding 35 years, some 140 papers had been published by “what may be regarded as two generations of investigators and their students” (Nelson et al., 1986, p. 8). In that report, which was prepared for delivery by the senior author at the First James L. Whittenberger Lecture at the Harvard School of Public Health, he reviewed the first studies of the influence of particle size in the lung at various respiratory rates and depths (Altshuler et al., 1957; Altshuler, 1959) and the first hollow airway cast studies to address the patterns and efficiencies of intrabronchial particle deposition.

To investigate where inhaled dust deposits in the lung and what happens after it deposits, volunteers inhaled monodisperse gamma-tagged radioaerosols in a prescribed breathing pattern (Nelson et al., 1986). The researchers detected retained particles with a ring of collimated scintillation detectors and a tracheobronchial region detector within a low background chamber to determine the thoracic burden of the inhaled radioaerosol. Using this method to track the time course of the deposited particles revealed short-term clearance from the tracheobronchial region and longer-term clearance attributed to the fraction deposited in the lower lungs. Clearance times, as well as fractional deposition as a function of particle size, could then be determined (Albert et al., 1969). When a single individual inhales particles of different sizes, the rapidly clearing fraction varies, providing a measure of the fraction of the inhaled particles that were deposited in the tracheobronchial region as a function of particle size (Figure 1).

Adaptation of this method to an animal model allowed demonstration of the effects of irritants such as SO₂ and cigarette smoke on lung clearance. The initial chosen animal model, surrounded by a counterweight-balanced
saddle holding the gamma-ray detectors, was large, patient, and cooperative (Figure 2). The data collected show increased clearance rates in a human volunteer and a donkey that resulted from smoking two cigarettes (Figure 3). An extensive list of additional NYU publications on regional deposition and clearance is provided in Nelson’s 1986 paper and includes a substantial body of work by Drs. R. E. Albert, M. Lippmann, R. B. Schlesinger, and others.

Figure 1. Retention of gamma-tagged monodisperse ferric oxide microspheres of various particle sizes (indicated in μm) for a single nonsmoking man participating in a series of inhalation tests. Fraction of inhaled particles cleared by mucociliary clearance varies systematically with particle size, but effective duration of bronchial clearance phase is relatively independent of size.
Source: Courtesy of M. L. Lippmann.

Figure 2. A donkey standing on a movable platform that permitted profile scanning of the thorax and head. The nasal catheters depicted here were used for delivering SO₂ vapor.
Source: Photo courtesy of M. L. Lippmann.
Approximately 160 aerosol-related publications have been added to the NYU-IEM bibliography since Nelson's original report. Many of these continued the use of monodisperse particles in hollow airway casts to provide detailed information about the deposition and distributions, along the airway paths, of coarse, fine, ultrafine, and fibrous particles.

Deposition studies in the first cast, with radioactively tagged insoluble particles, showed that areas of high deposition correspond to tumor sites in victims of primary lung carcinoma (Schlesinger & Lippmann, 1972). The cast was made from the airways of a human lung obtained at autopsy using the lost wax method. Subsequently, replicate casts were produced, and although the replication method limited the casts to airways greater than 3 mm in diameter, the replicates allowed for repeated measures of deposition for varied flow conditions, particle types, and particle sizes.

The first measurements in the replicate casts compared deposition of particles with diameters ranging from 3 to 8 µm for steady and cyclic inspiratory flow (Gurman et al., 1984). Deposition efficiency studies of fibers and their aerodynamic behavior followed (Sussman et al., 1991a), as well as measures of the deposition of ultrafine particles (Cohen et al., 1990).
Mathematical modeling of the replicate cast data for each of the parameters investigated provided insight into their deposition mechanisms and significance (e.g., Cohen & Asgharian, 1990; Sussman et al., 1991b). Using replicate casts, the enhanced deposition of ultrafine particles that results from particle charge could be demonstrated (Table 1) (Cohen et al., 1998).

### Table 1. Deposition of Charged Particles on Lung Airways

<table>
<thead>
<tr>
<th>Ratio of Deposition Efficiency</th>
<th>20 nm</th>
<th>125 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singly charged/charge neutralized</td>
<td>3.4 ± 0.3</td>
<td>2.3 ± 0.3</td>
</tr>
<tr>
<td>Singly charged/zero charge</td>
<td>5.3 ± 0.35</td>
<td>6.2 ± 0.7</td>
</tr>
<tr>
<td>Charge neutralized/zero charge</td>
<td>1.6 ± 0.3</td>
<td>2.7 ± 0.4</td>
</tr>
</tbody>
</table>

Source: Adapted from Cohen et al. (1998).

More recently, in collaboration with the University of Iowa (Dr. E. Hoffmann), it has been possible to produce hollow airway cast reproductions of living human tracheobronchial airways from images obtained by computerized tomography (Figure 4).

![Figure 4. Computerized-tomography-based, three-dimensional images of airway lumen. In vivo human lung (left panel); stereo-lithographic derived cast (right panel). Source: Photo courtesy of the author.](image-url)
Measurement Methods

Development of Measurement Methods

The original use of nonhygroscopic monodisperse particles for deposition studies revealed that at low levels of irritant exposure an acceleration of clearance rate is observed, whereas at higher doses and longer periods of exposure, the rate decreases (Nelson et al., 1986). This finding fostered further development of aerosol particle methods to study the lung, notably by Dr. E. D. Palmes and others at NYU. Deposition efficiencies of monodisperse particles were used, for example, to probe airway dimensions. In this method, an inhaled bolus of monodisperse particles is inserted at a selected position in the inhaled air stream, then a timed breath-hold is executed, followed by a forced expiration. The deposition efficiency measured as a function of breath-hold can be extrapolated back to zero breath-hold to give an estimate of the airway dimension (Figure 5).

![Figure 5. Comparison of the mean effective airspace diameters determined in excised lungs by using the aerosol breath-hold technique with the mean linear intercepts measured in the same lungs after inflation drying. Source: Lippmann (1990).]
Instruments
Over time, the execution of NYU-IEM research programs requiring measurement of exposure relevant to human health has led to the development of innovative samplers.

An Integrating Miniaturized Particle Size Sampler (IMP) (Figure 6) was developed for radon progeny measurement (Harley et al., 2005), to assess personal inhalation exposure at a former uranium processing facility in Fernald, Ohio. In this case, the goal was accurate assessment of exposure and dose from radon and decay products. The pilot aerosol particle size sampler (diameter = 4 cm, height = 3 cm) is fabricated from electrically conducting plastic and operates for up to 2 months, even in severe weather conditions. The sampler operates with a low flow pump (4–6 L/min\(^{-1}\)), and one version of the IMP has been tested for several years in all weather conditions. The present size spectrum covers from 1 nm to 10 µm. The particle size deconvolution is performed using extreme value estimation (EVE), a method developed at the University of Helsinki by Paati Pentero.

Figure 6. Integrating Miniaturized Particle Size Sampler (IMP). The sampler can have up to eight filtration stages. An impactor stage follows the inlet jets with size cutoff of about 2.5 microns. Six fine-mesh, stainless-steel screens (from 200 to 500 mesh) and an exit Millipore backup filter capture all residual particles not deposited on earlier stages.

Source: Photo courtesy of N. H. Harley.
An Integrating Diffusion Battery (Figure 7), also initially developed for radon progeny, uses porous discs and track etch detectors recessed smoothly into the walls of the diffusion tube. A flexible design version allows for varying the tube length and number of discs in the flow path.

![Integrating Diffusion Battery](image)

Figure 7. Integrating Diffusion Battery showing the porous plate collectors and the inserts used to hold collectors and track etch discs for detecting alpha particles emitted from the deposited particles. The unit may be assembled with as many sections as desired.


Additional samplers developed include a volatile aerosol sampler (Xiong et al., 1998a), a 14-day sequential PM filter sampler that proved useful in the aftermath of the World Trade Center collapse, and a unique method using iron nanofilms for measuring the ambient concentration of ultrafine sulfuric acid droplets (Cohen et al., 2000). In the latter, distinctive ringed reaction sites are seen when sulfuric acid particles react with a 19 nm thick iron coating on 0.5 cm square silicon chips. The chips are deployed in an electrostatic precipitator or a long, flat diffusion channel in an integrating parallel plate diffusion monitor developed specifically to hold the acid detectors. The number of reaction sites is assayed with a scanning force microscope (Figure 8).
World Trade Center

The resources of the NYU Aerosol Inhalation Laboratory permitted its personnel to respond promptly to the need for air quality measurements after the terrorist attack on the World Trade Center in 2001. They were able to obtain samples of deposited dust beginning on the evening of the disaster. The dust was separated into size fractions and analyzed for composition, including concentrations of asbestos and polycyclic aromatic hydrocarbons. The alkalinity of the dust was very high for the larger size fractions (pH > 10) but decreased for fine particles. The caustic nature of the coarse dust particles may explain the chronic cough seen in workers at the site and in area residents (Chen & Thurston, 2002).

To monitor the neighborhood air subsequent to the attack, an air sampling site with a variety of particle mass and size fractionating samplers was quickly established at the New York University Downtown Hospital. The site was about 1,000 m east of the World Trade Center (Chen & Thurston, 2002; Cohen et al., 2004a) (Figure 9). This site was the first one established in the area after the disaster and the closest to “ground zero.” The data (Cohen et al.,
2004a) for particle mass and number concentrations did not differ substantially from data collected in Manhattan the previous year. The dominant organic compounds found were those most common in urban environments. These data did not suggest, but cannot rule out, an unusual risk of adverse health effects from the number, or mass, of the fine ambient particles.

Figure 9. Samplers deployed at the New York University Downtown Hospital–World Trade Center sampling site from September 19, 2001, to December 20, 2001. The Lippmann 14-day filter sampler is at upper right.

MOUDI, micro-orifice uniform deposit impactor; MI, Mercer impactor; CNC, condensation nucleus counter; EAS, electrostatic aerosol sampler.

Source: Cohen et al. (2004a).

Occupational and Environmental Aerosol Research

Occupational Aerosols

Researchers at NYU interested in appropriate measurement of inhalation exposure have produced not only new measurement devices, but a number of studies dealing with biases that result from air sampling methods used to measure inhalation exposure. Early in the 1980s, they demonstrated that work clothing is a very effective scavenger of airborne-dust–containing contaminants and that resuspension of dust then becomes a contributor to the concentrations of contaminants in the breathing zone (Cohen et al., 1984). They also examined the problem of estimating solvent inhalation exposure for volatile aerosol droplets during spray application of polystyrene, such as in the manufacture of boats (Malek et al., 1986), and during automobile paint spray operations (Cohen et al., 1992). Cohen and colleagues reported that
up to 50% of the solvent is found in the droplets. Malek and colleagues also demonstrated the important effects of hood airflow disturbances caused by the presence of the worker in ventilated spray application processes.

Other recent aerosol studies at NYU-IEM have involved aerosols of metal working fluids, ZnO, endotoxin, cotton dust, cigarette smoke, cadmium oxide, and diesel exhaust. The studies aim to determine the adverse pulmonary and systemic effects of inhaled particles encountered in occupational and environmental settings. Recent years have seen the beginning of an active nanoparticle research program, including development of workplace sampling methods and the effect of coagulation on the toxicity of nanoparticles.

**Ambient Particulate Matter**
The ambient particle inhalation exposure program at NYU has integrated laboratory, field, and epidemiological studies. A few examples are noted here.

**Laboratory Studies**
A laboratory study of the hygroscopic growth of ultrafine particles with and without organic film coatings began to demonstrate the significance of the ambient organic mix in exposure to sulfuric acid. The study showed significant differences between the hygroscopic growth of pure sulfuric acid particles and those coated with a range of nanometer thick films of either lauric acid or stearic acid (Xiong et al., 1998b).

The results of an in vitro cell culture experiment that examined cellular response to exposure to a fixed mass of sulfuric acid aerosol demonstrated that response was enhanced when the mass was divided into smaller-sized particles (Chen et al., 1995). An increased adverse response, indicated by a decrease in internal cellular pH, was demonstrated when 300 µg m⁻³ of acid was subdivided onto a greater number of inert carbon core particles.

**Field Studies**
In one field study, researchers used a mobile laboratory designed for continuous measurements of concentrations of multiple air pollutants (Maciejczyk et al., 2004) that may have influenced the incidence of asthma in a community in the South Bronx. Another study of elementary school children with asthma employed a mobile van (Figure 10). The study found that exacerbations of symptoms and decline in lung function correlated most strongly with elemental carbon mass concentration, rather than the nonspecific fine particle mass (PM₂.₅). This ongoing innovative research
indicates that traffic-related pollution may be a significant factor in the respiratory health of such underserved inner-city populations (Spira-Cohen et al., 2006).

Figure 10. New York University mobile air sampling van at Public School 154 in the Bronx, New York.
Source: Photo courtesy of NYU Institute of Environmental Medicine.

Epidemiological and Chronic Exposure Studies
In 1999, under the direction of Dr. M. Lippmann, NYU became one of six national PM Centers funded by the US Environmental Protection Agency (EPA) to determine how exposure to unspecified ambient particles resulted in increasing mortality and morbidity in the United States. Developments under this program have been far reaching and dramatic.

Epidemiological research (with Brigham Young University) determined that ambient fine particles were responsible for much of the cardiac mortality and also for the lung cancer excess seen in the US population (Figure 11) (Pope et al., 2002, 2004). This demonstration of long-term adverse health effects of ambient PM spurred both subchronic animal studies and studies of source apportionment.
In the laboratory, mice were exposed to concentrated ambient particles (CAPs). Single exposures to CAPs were shown to increase the frequency of cardiac arrhythmias in aged male rats (Nadziejko et al., 2004). Subsequently, hyperlipidemic mice were exposed for 6 hours per day, 5 days per week, to concentrated ambient PM$_{2.5}$ for up to 5 months. The results, assessed by examining lesions (plaque) in the aortic sinus regions, showed acute and chronic effects of fine particles on the cardiovascular system (Chen & Nadziejko, 2005).

Source Apportionment

Demonstration of the association between long-term exposure to fine particulate matter (PM$_{2.5}$) air pollution and increased risk of mortality, noted earlier, leaves the question of which pollution source emissions are most damaging. In 1999, EPA instituted a nationwide PM$_{2.5}$ mass and composition Speciation Site Network that provides the PM$_{2.5}$ characteristics needed to conduct a statistical apportionment of air pollution impacts for cities across the United States. It was also demonstrated that source apportionment methods are reliable for apportioning the health effects of PM$_{2.5}$ (Thurston et al., 2005).
Using the 2000–2003 EPA Speciation Site Network data, Thurston and Lall (2006) conducted a factor analysis of the entire nation to apportion PM$_{2.5}$ to source categories and locations around the United States. The sources identified (and their key elements) were the metals industry (Pb, Zn); soil particles (Ca, Si); motor vehicles (OC, EC, NO$_3$); the steel industry (Fe, Mn); coal combustion (As, Se); oil combustion (V, Ni); salt particles (Na, Cl); and other sulfate (S). These sources represent over 80% of the US mean PM$_{2.5}$. Thurston and Lall’s results indicate that applying source apportionment methods to the EPA Speciation Site Network can be a useful avenue to identify sources affecting the nation and to determine source-specific health effects, thus allowing more efficient regulation of PM$_{2.5}$.

Identification of Specific Toxic PM Components
Cardiovascular effects have recently been linked to the presence of nickel in ambient air in mice, as shown in the chronic exposure experiments carried out with CAPs, and have also been observed in people (Lippmann et al., 2006). In the mouse chronic exposure study, they established that excursions of heart rate occurred on days with elevated concentrations of nickel in the PM$_{2.5}$. They were able to use back trajectories to establish a specific source of nickel for those days. They then established support for the hypothesis in two human populations: (1) by reanalysis of the National Mortality, Morbidity, and Air Pollution Study (Figure 12) and (2) by reexamination of a report of reduced mortality in a Hong Kong intervention to reduce sulfur concentrations in fuel, which also led to reduction in ambient nickel concentrations (Lippmann et al., 2006).

![Figure 12. Differences in mortality risk coefficients per the 5th- to 95th-percentile difference in fine particulate matter (FPM) and FPM components across the National Mortality, Morbidity, and Air Pollution Study metropolitan statistical areas (MSAs) for the 60 MSAs for which FPM speciation data were available. Source: Adapted from Lippmann et al. (2006).]
Summary
More than 50 years of health-related aerosol research at NYU, beginning at the interface of airborne particles and the respiratory system, have resulted in a wealth of knowledge about the interaction of airborne particles and people. This knowledge has supported efforts to reduce the potential for harm when people are exposed to toxic airborne particles occupationally or environmentally.

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References


