Toxicologic and Epidemiologic Clues from the Characterization of the 1952 London Smog Fine Particulate Matter in Archival Autopsy Lung Tissues

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Exposure to atmospheric fine particulate matter (PM), even at low ambient concentrations, has clearly been linked to increases in mortality and morbidity. A 10-μg m^{-3} increase in PM_{10} (PM < 10 μm) has been found to produce a 0.5% increase in daily mortality. The mechanism of action is a source of debate, although recent attention has focused on the cardiac effects of PM exposures. Likewise, several possible etiologic agents have been implicated, including ultrafine PM (PM ≤ 100 nm), metals, and the acid components, yet the responsible constituent remains undetermined. During the catastrophic PM exposure episode in London in December 1952, some 4,000 excess deaths occurred at the height of the event. The extreme mortality during that episode and the preservation of archival autopsy tissues allow us the unique opportunity to report on the form and composition of December 1952 London PM *in situ* in tissues from persons known to have died from the smog exposure. Because absolute increases in mortality with current levels of PM in Western Europe and North America are low, analogous tissues are unlikely to be contemporaneously available. Taking a lung compartment (airway, airspace, interstitium, and lymph node) approach, we differentiated exposures contemporary with death from those of earlier origin. Electron microscopic analyses revealed the dominance of retained soot and a surfeit of other particle types. A variety of metal-bearing particle types were found in all compartments, but Pb, Zn, and SnZn types appeared the least biopersistent. The results support the acute toxicologic importance of ultrafine carbonaceous and metal PM. *Key words:* 1952 London smog, autopsy, lung pathology, metals, mortality, particulate matter, scanning electron microscopy. *Environ Health Perspect* 111:1209–1214 (2003). doi:10.1289/ehp.6114 available via *http://dx.doi.org/* [Online 5 March 2003]

As a result of a series of studies in the early 1990s, it became evident that a consistent link exists between daily mortality and particulate matter (PM) air pollution even at low PM levels. In the Harvard Six Cities Study, it was demonstrated that the residents in the cities with the lowest PM levels had a survival rate roughly 2 years longer than those living in the cities with the highest PM levels (Dockery et al. 1993). These results were confirmed by the American Cancer Society Cancer Prevention Study II (Pope et al. 1995) with a much larger study population (1,200,000 adults). Following the subsequent promulgation of a new national PM standard [U.S. Environmental Protection Agency (U.S. EPA) 1997], and a challenge to that standard by the American Trucking Association (*American Trucking Associations Inc. v. United States Environmental Protection Agency* 1999), these results came under considerable scrutiny. A Health Effects Institute reanalysis of the data (Krewski et al. 2000) showed the data to be of high quality; the original results were replicated and the results were found not to be sensitive to alternative statistical methods. Confirmation of the importance of PM exposure has been provided by the National Morbidity and Mortality Air Pollution Study. The study found that gaseous copollutants as a time-varying factor do not confound or modify the association of particulate air pollution with mortality (Samet et al. 2000b). Weather and climate as time-varying factors also appear not to confound or modify the relationship between PM and mortality (Samet et al. 1998). Time-series analysis of daily mortality pooled across 20 U.S. cities (1987–1994) showed a 0.5% increase in daily mortality associated with each 10 μg m^{-3} increase in PM_{10} (Samet et al. 2000a). Moreover, the dose response for mortality and PM exposure seems to be linear, with a response even at the lowest exposure concentrations (Schwartz and Zanobetti 2000). The effect is also not a result of harvesting because there is no evidence that PM_{10} is advancing date of death by only a few days (Schwartz 2000). So strong has the evidence relating PM and mortality become that in a recent editorial statement in *Epidemiology*, Samet (2002) noted, "by recent count there have been 110 papers on time-series studies of particulate air pollution and daily mortality. . . . In the context of this abundant literature, what can yet another study add?" Yet the responsible PM agent(s) remains elusive, and the biologic mechanism of action is still uncertain.

Three acute PM exposure–linked mortality events that occurred in the last century have often been recognized as the spur for this recent PM research (e.g., Wilson 1996). These historic exposure episodes occurred in the Meuse Valley (Belgium) in 1930, in Donora, Pennsylvania (USA), in 1948, and in London in 1952. Although the smog episodes that took place in Donora, which resulted in 20 fatalities (Helfand et al. 2001; Schrenk et al. 1949), and the one that occurred in the Meuse Valley, which produced 60 fatalities (Firket 1936; Nemery et al. 2001), are landmark air pollution events, the London episode caused much greater loss of life. Some 12,000 fatalities have been attributed to the 1952 smog.

The city of London has had a long history of air pollution problems, and episodic smogs associated with increases in human mortality that can be traced back to the seventeenth century (Brimblecombe 1988). During the last century, the number of smog events declined to a fraction of those that occurred at the peak period at the end of the nineteenth century; however, such events continued to occur until the last decade of the century (Brown 1994). Many of these episodes had a major impact on the health of the population of London. Major events occurred in November 1948 (700–800 fatalities), January 1956 (1,000 fatalities), December 1957 (750 fatalities), January 1959 (200–250 fatalities), and December 1962 (340–700 fatalities). These events have been well documented (Bradley et al. 1958; Logan 1949, 1953, 1956; Martin 1961; Scott 1963). However, the smog event of 1952 was, in terms of human health effects, the most calamitous of the century. It is the sentinel event of the century linking PM exposure to excess mortality and morbidity. The committee on air pollution that reported on the episode (Beaver 1953) estimated that the number of deaths coincident with the smog totaled 4,000 more than that normally expected. Recent estimates suggest that, with the additional persisting effects of the smog, there were a total of 12,000 excess deaths between December 1952 and February 1953 (Bell and Davis 2001).

The smog event lasted 5 days (5–9 December 1952) and was of considerable intensity. Smog conditions over London are

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characterized by stagnant air masses trapped by a temperature inversion that produces a shallow mixing layer with little horizontal or vertical air movement. Typically, this is the product of an anticyclonic system covering Western Europe with high barometric pressures and low-pressure gradients. During the first week of December 1952, a slow-moving high-pressure system became stationary over London and persisted for several days. Particulate emissions from domestic fires and industrial processes provided condensation nuclei for the moist air to form dense smog. With little atmospheric dispersion, as the event progressed the SO_2 and smoke levels climbed to peak values of 3.83 and 4.46 mg m^{-3} respectively. The typical winter situation of high pollutant levels was exacerbated by increased emissions from domestic heat sources and power plants because of atypically low temperatures (daily mean temperatures were below the 80-year average). Besides releases from the combustion of coal, oil, and coke, plus products from various industrial activities, the London atmosphere was also burdened with unprecedented levels of diesel emissions. This was a consequence of the introduction of thousands of diesel-powered buses as replacements for electric trams phased out in London by July 1952.

In terms of adverse health effects, the older members of the population of London were disproportionately affected by the smog exposure. The average number of weekly deaths for the 0- to 25-year-old group rose from 46 (weekly average) in November to 74 at the height of the episode (for the week ending 13 December 1952). In comparison, the increase in mortality for individuals more than 75 years old was from 477 to 1,666. The most important causes of death during the week at the episode's height (7–14 December), according to death certificate data (Beaver 1953), were bronchitis (a 14-fold increase over the November weekly average), influenza (a 12-fold increase), pneumonia (a 5-fold increase), other respiratory diseases (a 9-fold increase), and heart disease (a 3-fold increase). It is noteworthy that those listed as "influenza" have recently been determined *not* to be due to influenza, because there was no demonstrated influenza epidemic at the time (Bell and Davis 2001).

The 1952 smog stimulated extensive expansion of aerosol sampling in London and elsewhere, but actual sampling of the PM comprising the December 1952 aerosol was minimal, and to our knowledge no archival samples from that episode are available for analysis using modern techniques. We hypothesized that the archived preserved lung tissues from persons dying at the time of the epidemic would contain inhaled and retained PM representative of the December 1952 PM (the lung PM record), and that by characterizing the form and composition of the PM in various microscopic compartments of the lung, we might obtain otherwise unavailable information relevant to exposures related to the high mortality observed. We felt such data should also be valuable for comparison with current epidemiologic, toxicologic aerosol chemistry, and public health investigations.

We also recognize that contemporary attempts at collection of actual human lung tissues from persons known with high probability to have died as a result of PM exposures would be exceedingly unlikely to succeed. Massive mortality events such as that in London in 1952 no longer occur, and because of the dramatic decline in the frequency of autopsies, the likelihood of obtaining tissue from persons dying from effects of high PM is diminished.

Materials and Methods

To test the hypothesis that archived lung tissue would preserve a record of the historic aerosol, we initially reviewed autopsy records for selected years in the 1950s and 1960s at the Royal London Hospital (RLH) to determine the availability of suitable material. This was facilitated by the fact that during the 1950s and 1960s, the autopsy rate at the RLH was > 60%, with > 400 autopsies/year. Our review focused on two sensitive populations: infants (< 1 year) and older people (> 45 years) with autopsy diagnoses including either chronic obstructive pulmonary disease (COPD) or congestive heart failure. Available slides from suitable cases were reviewed and classified regarding organ; if lung, they were further classified regarding portion of lung where located and were screened to identify which histologic compartments were sampled. All cases contained some fine opaque particles that could not be chemically analyzed by light microscopy. After this initial review, if tissue blocks were available containing lung or lymph node, they were retrieved from the archive for further study.

To study the airborne PM inhaled by the smog victims, we conducted a histopathologic and microanalytic examination of available tissue. Standard pathology laboratory preparations for light microscopy and electron microscopy were used. For preexisting specimens, paraffin blocks of formalin-fixed tissues were sectioned at 5 μm, and sections were stained with hematoxylin and eosin (H&E) for routine pathologic evaluation. Sections for electron microscopy analyses were mounted on pure carbon support medium, and the paraffin was removed with xylene before analysis. Microanalysis of tissue-retained PM was by scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDX) (Abraham and Burnett 1983). Light microscopy and backscatter electron (BE) imaging by SEM identified retained PM, and the compositional characteristics of the individual particles were established by EDX. We used a Hitachi S-520 SEM with Princeton Gamma-Tech Integrated Microanalyzer for Images and X rays (IMIX) system (Princeton Gamma-Tech, Princeton, NJ), and a Hitachi high-resolution field emission SEM (model 8400; Princeton Gamma-Tech). Two methods of sizing were used in the analysis. Individual inorganic particles were sized by the analyst with reference to a calibrated marker on the SEM image. Cross-sectional areas were determined using IMIX image analysis software after converting the captured digitized images into binaries of the projected areas.

We also employed an *in situ* lung compartment approach that targeted four specific compartments [focusing on PM found in airway exudates, macrophages (MΦ) in the airspaces (airspace-MΦ), interstitial-MΦ, and lymph

Table 1. London smog deaths with analysis of autopsy tissue, by demographics and cause of death.

Case	Date of death	Age (years)	Sex	Diagnosis 1	Diagnosis 2
1	7 Dec	76	F	Heart failure	Bronchitis
2	23 Jan	61	M	Bronchitis[a]	Emphysema
3	3 Dec	65	M	Pulmonary embolism	Lung cancer
4	6 Dec	53	M	Heart failure	Bronchitis
5	10 Dec	20 hr	M	Prematurity	
6	12 Dec	54	F	Emphysema	Hodgkin's disease
7	17 Dec	51	F	Sarcoidosis	
8	19 Dec	53	M	Heart failure	Bronchitis
9	25 Dec	51	M	Pneumonia	Tubercular meningitis[a]
10	4 Jan	60	M	Heart failure	Syphilitic aortitis
11	6 Jan	62	F	Heart failure	Emphysema
12	12 Jan	6 months	F	Pneumonia	Possibly cystic fibrosis
13	14 Jan	55	M	Bronchitis[a]	Gastric ulcer
14	17 Jan	64	F	Esophageal cancer	Aspiration
15	23 Jan	44	F	Bronchitis[a]	Pneumonia
16	28 Jan	62	F	Lung abscess[a]	
17	12 Feb	61	M	Heart failure	Bronchitis
18	5 Mar	66	M	Emphysema[a]	Myocardial infarction

Abbreviations: Dec, December; F, female; Feb, February; Jan, January; M, male; Mar, March.
[a]Autopsy note: condition worsened during smog.

node-MΦ]. This compartmentalization allowed inhaled PM to be separated on retention time, with lung residence time increasing along the following path:

airways < airspace macrophages
< interstitial macrophages
< lymph node macrophages.

Such differentiation is lost when bulk samples of tissue are used to quantify the retained lung burden (Tsuchiyama et al. 1997).

Two basic particle forms were identified in the electron microscope. The most common was a low-atomic–number (< 11) feature of consistent composition present in large aggregates (carbonaceous material). Less common were higher-atomic–number (≥ 11) particles of variable composition (noncarbonaceous) found interspersed in the less dense aggregates. Noncarbonaceous PM was compositionally characterized on a particle-by-particle basis by EDX analysis. Areas of tissue corresponding to dusty areas seen in the light microscopic sections of the four compartments were imaged in the SEM. Consecutive individual particles in aggregates or dust-laden MΦ were identified by BE imaging, and the size and composition of each were recorded. Sections were reviewed until data on a minimum of 500 particles per compartment were collected or until all available material was analyzed. To achieve this total, in most cases several sections were examined. The subsequent grouping of particles into specific type classes was based on the associations of the major elements in the particles. Two basic categories of particle type classes were operationally defined: "heavy metal" and "other inorganic." The former consisted of those classified as Pb type (±Ca, and/or P), Sn type (containing predominantly Sn), Zn type (composed almost exclusively of Zn), SnZn type, Sb-containing type, SbPb type, and "other metal" particles (Cu-, Ni-, Cd-, or Mn-containing). The "other inorganic" types were designated as Fe type (composed exclusively of Fe), Fe-plus type (Fe was the dominant element), Ti type (Ti-bearing), Si type (composed exclusively of Si), SiAl type (composed of SiAl), SiAl-plus type (SiAl were the dominant elements), or "other types" (Ba-, Ca-, or Al-bearing). The heavy metal designation defines respirable particles that are anthropogenic in origin. The other inorganic classification is an assignment given to particles that are likely to be of nonanthropogenic origin. Clearly, some particles assigned to types in the latter category will be of anthropogenic origin (e.g., Fe type, and Ti-rich); however, these types have been retained in the other inorganic category because of the possibility that they may have been derived from natural sources.

Here we present data on the quantity of exogenous PM (on a compositional basis) in tissue samples from 16 individuals who expired at the time of the 1952 smog. Additional extensive examination of specimens from two infants (20 hr and 6 months old) failed to document readily quantifiable amounts of exogenous PM in these cases. The dates of death of the 16 study subjects were between 3 December 1952 and 5 March 1953. Subject ages ranged from 44 to 76 years old (median 60.5); seven were female. All were selected by cause of death as COPD (or other respiratory disease) or heart failure on the original autopsy report. Details of date of death, cause of death, and subject demographics are listed in Table 1.

Results

An extensive review of the autopsy records at the RLH revealed a doubling of the number of reports listing COPD as a major finding during December–February 1952–1953 compared with other comparable periods. For these months for the years 1951–1952, 1952–1953, 1953–1954, 1955–1956, and 1962–1963, the RLH autopsies recorded 12, 23, 13, 9, and 13 cases, respectively, documenting COPD.

The microanalysis of lung tissue revealed that the common feature of the exogenous PM in all lung compartments reviewed in the study cases from the 1952–1953 period was an aggregation of very fine carbonaceous material (unit size ≤ 0.1 μm) associated with a variety of fine (generally ≤ 1.0 μm) inorganic particles. Limited availability of material did, however, preclude the analysis of every one of the specified compartments in all cases. Airway aggregate PM was identified in two of the cases, airspace-MΦ–bound PM in five cases, interstitial-MΦ–bound PM in 15 cases, and lymph node-MΦ–bound PM in two cases. In all, nearly 8,000 individual particles were characterized by SEM/EDX.

The airway-confined, but cell-free, sooty aggregates were identified in conjunction with mucopurulent exudate (Figure 1; case 1). SEM-based BE imaging (i.e., atomic number contrast imaging) of these aggregates revealed substantial quantities of denser particles in the low-density matrix (Figure 2; case 2). Higher magnification, field emission, SEM imaging of this matrix revealed an agglomeration of mucus-enmeshed spheroidal particles resembling chain aggregates of carbonaceous particles (Figure 3; case 2). The aggregates ranged from approximately 0.004 to 0.009 mm^2 in cross-sectional area. Analysis of seven sections of aggregate from case 1 and two sections of two aggregates from case 2 identified between approximately 100 and 850 noncarbonaceous particles per aggregate per section. Most of the analyzed inorganic particles were heavy-metal type (containing Pb, Zn, Sn, Fe, Sb, and occasionally Mn, Cu, or Cd), and the remainder were classified as "other inorganic" type.

Similar mixtures of carbonaceous and noncarbonaceous PM were identified in airspace-, interstitial-, and lymph node-MΦ. That is, in each of these compartments inorganic particles of various compositions were found interspersed in the carbonaceous matrix. This is illustrated in Figure 4, which documents PM-laden interstitial-MΦ from case 1. Low-magnification SEM imaging of the interstitial-MΦ (Figure 5) and higher magnification BE imaging (Figure 6) revealed

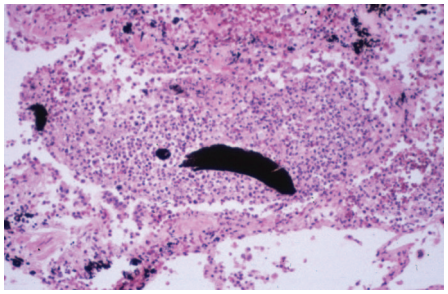

Figure 1. Light micrograph (H&E stain) showing bronchiole (~300 μm in diameter) with mucopurulent exudate containing aggregate of opaque PM from case 1. Magnification approximately 100×.

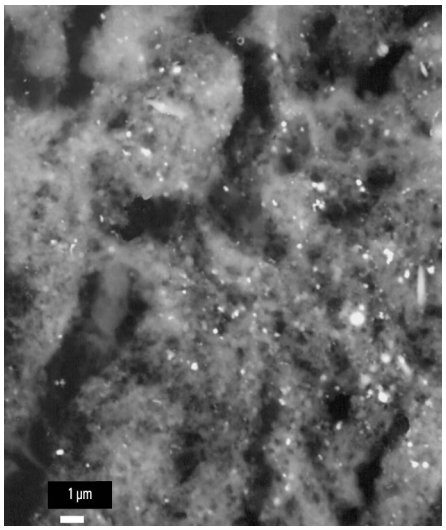

Figure 2. BE micrograph of section of airway aggregate from case 2 revealing abundant submicrometer inorganic (bright) particles.

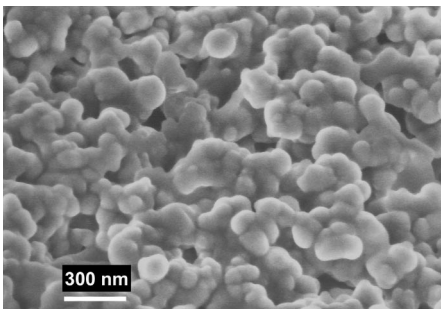

Figure 3. High-magnification field emission scanning electron micrograph of airway aggregate from case 2 showing ultrafine PM structure.

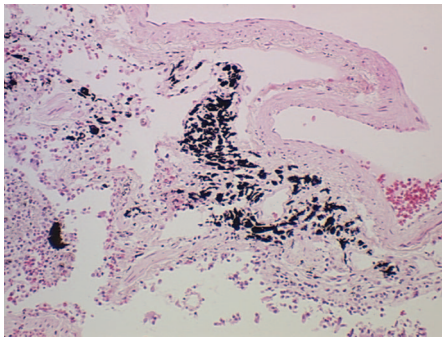

Figure 4. Light micrograph (H&E stain) showing interstitial macrophages from case 1 with opaque PM. Magnification approximately 100×.

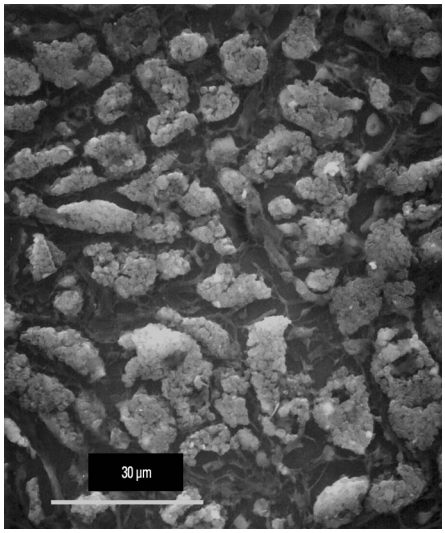

Figure 5. Scanning electron micrograph of interstitial macrophages from case 1 loaded with an abundance of PM.

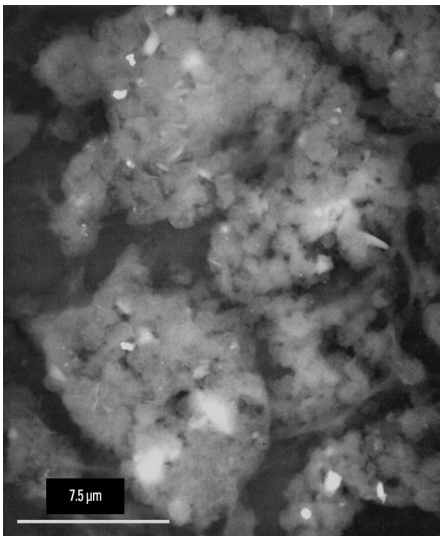

Figure 6. BE micrograph detail of Figure 5 of interstitial macrophages containing numerous inorganic (bright) particles.

a heavy PM loading and inorganic particle content consistent with the airspace- and lymph node-MΦ compartments. Analysis of airspace-MΦ particles identified a less diverse range of "heavy metal" particles (containing predominantly Zn, Sn, and Fe, but rarely Sb, Mn, or Pb) than was observed in the airway-aggregate compartment. In the interstitial- and lymph node-MΦ compartments, the "heavy metal" particles occurred less frequently than in the airway-aggregate compartment. Because of the presence of fewer "heavy metal" particles in the airspace-, interstitial-, and lymph node-MΦ compartments, the "other inorganic" dominated these assemblages.

The compositional analyses of retained particles showed interesting intercompartmental differences. The clearest differences were observed in those cases for which multiple compartment identification was possible. In those cases (1 and 2) with airway PM aggregates, the inorganic PM assemblage differed markedly between the first and the other three compartments (Figure 7). In these cases, half of the inorganic PM analyzed in the airway aggregates was categorized as "heavy metal" particles. In this compartment, the Pb-, Sn-, and ZnSn-bearing particles dominated. In the other compartments in these cases, the Pb- and ZnSn-bearing types were almost completely absent (Figure 7A). In contrast, all particle types in the "other inorganic" particle category were represented in each compartment (Figure 7B). This suggests that these essentially nonmetallic particles were not selectively removed. This pattern was repeated in the nonairspace aggregate compartments of the other cases. In each, the Pb- and ZnSn-bearing types were not extensively identified in the airspace-, interstitial-, and lymph node-MΦ compartments (Table 2).

Discussion

Our analysis of the London autopsy lungs revealed a number of important findings about PM exposure of the study population. First, our survey of autopsy records demonstrated a peak of COPD-related deaths during the times of the reanalysis of London mortality data by Bell and Davis (2001). The analysis suggests that aggregated PM (cell-free, or exudate-trapped) in lung airways reflects the most recent inhalation exposure of the subjects. We view such PM in the lung as having been retained contemporaneously with the 1952 smog event. The PM content of the other compartments we consider representative of progressively earlier exposures. PM in interstitial-MΦ, in perivascular and peribronchiolar locations (the "sump" of regional clearance), and in lymph node-MΦ represent much longer residence times. We consider it unlikely that London residents were exposed to some new PM source during the smog event; rather, they were subject to an increased dose of the typical exposure aerosol. However, increased levels of diesel PM were probably present in the London aerosol following the final conversion of public transport from trams to diesel buses in the summer of 1952 (King and King 2002). We suggest that intercompartmental differences in PM content should largely be related to the duration of retention in the lung. Although a carbonaceous PM component was a feature of each analysis compartment, other inorganic PM components were not constant. Most notably, certain heavy metal–bearing particle types that are abundant in the most recent retention compartment (e.g., Pb, ZnSn in the airway aggregates) are almost totally absent from the longer-term storage compartments. We suggest that such changes in PM content are a response to variations in metal solubility. If soluble components of PM affect physiologic processes, metal solubility may be a factor in PM-mediated mortality and morbidity. Our results also cannot exclude the rapid transport from the lung of fine and ultrafine carbonaceous particles (from coal-burning and diesel sources) because there are no demonstrable

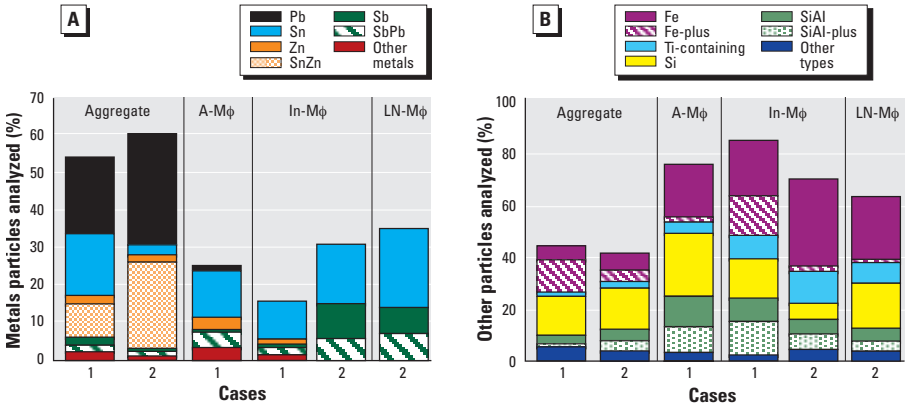

Figure 7. Bar graphs of the relative proportions of inorganic particle types in each lung compartment analyzed in cases 1 and 2 (as a percentage of the total number of particles characterized in each compartment in each case). Metal type particles in the airway aggregate (Aggregate), in the airspace macrophages (A-MΦ), in the interstitial macrophages (In-MΦ), and in the lymph node macrophages (LN-MΦ) are presented separately (*A*) from the other inorganic particle types (*B*).

Table 2. Percentage of retained heavy metal and other PM in different lung compartments of 15 individuals who expired at the time of the 1952 London smog (excluding cases 1 and 2).

	Airspace-MΦ Case no.				Interstitial-MΦ Case no.													Lymph node MΦ Case no.
Particle type	9	10	13	16	3	4	6	7	8	9	11	13	14	15	16	17	18	14
Pb	0	0	< 1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sn	< 1	4	11	4	5	40	1	1	19	4	15	8	6	2	6	13	13	4
Zn	5	2	2	3	1	1	3	3	0	1	2	1	0	2	0	2	0	< 1
SnZn	0	0	0	< 1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Sb	2	0	2	< 1	0	1	0	0	2	0	0	1	1	0	0	0	1	< 1
SbPb	1	3	2	1	1	15	0	0	14	1	5	2	2	0	1	4	7	< 1
Other metal	4	2	4	2	0	0	1	0	3	1	0	2	2	0	1	1	1	< 1
Other particles	88	89	79	88	93	42	95	96	62	91	78	86	89	96	92	80	78	95
Particle total[a]	250	275	500	500	121	250	500	500	500	500	500	500	500	500	500	500	500	500

[a]Total number of inorganic particles, including the non-"heavy" metal particle types analyzed in each case.

compositional differences that could be detected by the EDX methodology. Similarly, although the methodology provides information on individual particle speciation, it cannot supply data on the concentrations of the inorganic elements present in each compartment. Therefore, we have not been able to assess in a quantitative manner the mobilization of individual metals. Also, the analysis could provide no information on possible material loss during the original fixation and embedding process, but we imagine such a loss would apply to all our defined compartments.

Recent studies have shown that lung inflammation is mediated by water-soluble components of common atmospheric constituents such as residual oil fly ash (ROFA) (Dreher et al. 1997). The importance of soluble metal components in ambient air has been reinforced by experiments with historic PM from the Utah Valley using healthy human subjects (Ghio and Devlin 2001). A marked inflammatory response was induced when extracts with the highest soluble metal content (most notably Zn), were administered. Interestingly, soluble Zn (a metallic element and a PM constituent that we find not to be significantly retained beyond the airway aggregates) has been identified (rather than any other metal component) as the cause of cell injury in animal exposure studies (Adamson et al. 2000).

The importance of metal-containing PM in relation to cardiovascular health effects has also been demonstrated in several studies. ROFA, with its high metal content, has been shown to produce systemic inflammation. Decreased plasma lymphocyte levels have been observed in exposed rats (Kodavanti et al. 2002). Elevated levels of plasma fibrinogen have also been produced in ROFA-exposed rats (Gardener et al. 2000; Kodavanti et al. 2002). This material produces acute depression in S-T segment area in exposed rats (Kodavanti et al. 2000), and S-T inversions in compromised (monocrotaline-treated) rats (Costa and Dreher 1997). Severe arrhythmias have also been observed in compromised rats (Costa and Dreher 1997), and bradycardia in dogs (Muggenburg et al. 2000) exposed to ROFA.

Similar outcomes have been observed after exposure to ambient PM. Systemic inflammation effects are observed in individuals exposed to PM, including elevations of C-reactive protein and decreases in red blood cells (Peters et al. 2001; Seaton et al. 1999). Increased plasma fibrinogen levels have been reported in association with ambient PM exposure (Prescott et al. 2000; Schwartz 2001; Seaton et al. 1999) and with concentrated ambient particle exposures (Ghio et al. 2001). Increased PM exposure also appears to be associated with increases in blood viscosity (Peters et al. 1997). Heart rate changes have been positively associated with ambient PM exposure (Peters et al. 1999; Pope et al. 1999), although a negative association has also been observed (Gold et al. 2000). Decreased heart rate variability seems to be associated with PM exposure in elderly populations (Gold et al. 2000; Liao et al. 1999; Pope et al. 1999). In animal models, heart rate decreases have been recorded in dogs exposed to concentrated ambient particles (Godleski et al. 2000) and in aging rats exposed to PM from the Ottawa aerosol (Watkinson et al. 2001). Increased arrhythmias have also been documented in the Ottawa PM–exposed rats (Watkinson et al. 2001). Perhaps most significant, increased defibrillator discharges have been associated with PM exposures (Peters et al. 2001), and the risk for myocardial infarction onset increases with PM exposure 2 hr before the myocardial infarction (Peters et al. 2002).

Perhaps an unsurprising finding of this study was the identification of a substantial burden of Pb PM in the lung airway aggregates. Because lead as a fuel additive has been greatly reduced or eliminated, little current toxicologic research related to PM has focused on the role of Pb. However, Pb is still used as a gasoline additive in many countries. Given that Pb is one of the predominant PM metals observed here, it may be that Pb deserves more study. A recent analysis of aerosols in Boston (Godleski et al. 2002) indicates a strong correlation between Pb and adverse health effects in animal subjects. The consistent identification of Sb-bearing particles is more surprising. The origin of this PM component is uncertain, although coal-fired plants, incinerators, and smelters are all possible sources. Elevated levels of Sb in the London aerosol is supported by evidence of high concentrations of Sb in London street dust (Fergusson and Ryan 1984).

In conclusion, we have located and analyzed rare archival tissue samples that provide otherwise unavailable clues to the nature of the fatal PM exposures in the 1952 London smog. The evidence regarding ultrafine carbonaceous and metallic PM is valuable both in supporting current and in suggesting additional epidemiologic hypotheses and toxicologic investigations.

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