It has been assumed that damage from exposure to tobacco smoke and other particulate air pollutants is imposed primarily on the lungs and is associated with increased morbidity and mortality rates in patients with preexisting lung disease. This is supported by a considerable amount of previous data, such as the mortality data from the December 1952 London smog disaster, which may have caused as many as 12,000 deaths, almost all in patients with preexisting lung disease. Total suspended particulate matter (PM) was as high as 3000 μg/m³. Similar patterns of elevated morbidity and mortality rates, primarily in patients with preexisting lung disease, have been documented in other acute episodes of air pollution in the past. However, evidence from the past 10 years shows that sudden increases in ambient air pollution can also rapidly raise morbidity and mortality rates in patients with existing cardiovascular disease, as much or more than the rise associated with lung disease. In the present issue of Circulation, Pope and associates report interesting new data on the effects on mortality of an appropriate surface for efficient removal by macrophages. Thus, chronic particle retention and tissue remodel-
Radioactively labeled colloidal albumin in hamsters.\textsuperscript{9} into blood is reported after tracheal instillation of ultrafine, lung parenchyma.\textsuperscript{6,7} After inhalation, ultrafine carbon particles are rapidly removed by a combination of phagocytosis, diffusion or are breathed back out again without deposition. They are rapidly removed by a combination of phagocytosis, lymphatic flow toward hilar nodes, and capillary blood flow, and they appear to not be retained in large numbers in the lung parenchyma.\textsuperscript{6,7} After inhalation, ultrafine carbon particles that have been radioactively labeled can be detected in blood within a minute and reach peak concentrations in peripheral blood within 10 to 20 minutes.\textsuperscript{8} Similar transport into blood is reported after tracheal instillation of ultrafine, radioactively labeled colloidal albumin in hamsters.\textsuperscript{9}

Importance of Particle Size on Risk of Death From Air Pollution

Ultrafine particles probably are capable of causing much greater tissue damage than larger particles when deposited and may be the greatest source of elevated risk for death from ischemic heart disease or fatal arrhythmia. The lungs seem to provide rapid transport of these potentially damaging particles from inspired air to circulating blood. This is consistent with the significant increase in risk of triggering a myocardial infarction within 1 to 3 hours of a sudden increase in fine particulate pollution (d\textsubscript{p} < 2.5 \textmu m), and the increased risk may persist several days after the exposure.\textsuperscript{10} Increases in concentration of PM\textsubscript{2.5} particulates also have been noted to cause mean heart rate to increase and to depress heart rate variability, suggesting altered autonomic control, which may be associated with higher risk of cardiac arrhythmias.\textsuperscript{11,12}

Diesel exhaust fumes are made up largely of fine and ultrafine carbonaceous particulates generated in smokers.\textsuperscript{5} Particles \leq 0.1 \textmu m diameter are referred to as \textit{ultrafine} and aerodynamically are too small to sediment out during normal breathing; however, they are deposited on alveolar walls by diffusion or are breathed back out again without deposition. They are rapidly removed by a combination of phagocytosis, lymphatic flow toward hilar nodes, and capillary blood flow, and they appear to not be retained in large numbers in the lung parenchyma.\textsuperscript{6,7} After inhalation, ultrafine carbon particles that have been radioactively labeled can be detected in blood within a minute and reach peak concentrations in peripheral blood within 10 to 20 minutes.\textsuperscript{8} Similar transport into blood is reported after tracheal instillation of ultrafine, radioactively labeled colloidal albumin in hamsters.\textsuperscript{9}

Effects of a High Incidence of Smoking in the Population at Risk

In the study reported in this issue of \textit{Circulation} by Pope et al,\textsuperscript{3} risk of death from different causes in response to increased pollution has been separated into that collected from “never,” past, and current smokers (see Tables 4 and 5 in Pope et al\textsuperscript{3}). Data from these tables summarize the most important and interesting observations from the article. Relative risk of death from cardiovascular and lung disease becomes reversed in magnitude between never smokers and current smokers. The difference is very large; risk of death from lung disease in current smokers increases by an order of magnitude compared with never smokers. In Table 2 of the present editorial, these data from Pope et al\textsuperscript{3} are compared with the mortality data from the 1952 London smog disaster summarized by Schwartz.\textsuperscript{2} Results from the 1952 London smog were not adjusted for smoking. Smoking undoubtedly was more prevalent in 1952 than in the 1980s, when the data reported by Pope et al were collected. Elevated risk ratios for death from COPD in current smokers from Table 4 of Pope et al\textsuperscript{3} are very similar to the fold increase in death from COPD in the London smog of 1952. When adjustment is made for current or past smoking, risk of death from lung disease falls to nothing or reverses. In patients with COPD, a risk ratio significantly less than 1.0 for death from COPD does not mean that air pollution is protective; more likely, it means that more of these patients are dying from pneumonia or from cardiovascular complications.

Short-Term Versus Long-Term Studies

In short-term studies of mortality from sudden increases in air pollution, recorded causes of death may represent premature triggering of an event that was about to happen anyway in patients with preexisting lung or cardiovascular disease. These short-term increases in mortality rate in response to transient increases in air pollution do not provide clear information on the role of air pollution on the natural progression of the disease, such as would be provided by a chronic elevation of blood cholesterol or a chronic smoking history. The study reported by Pope et al\textsuperscript{3} is a long-term study, comparing effects of differences in average quarterly pollution levels among metropolitan regions on causes of...

<p>| TABLE 1. Standard Description of Inhaled Pollutants |
|---------------------------------|--------|---------------------------------|--------|</p>
<table>
<thead>
<tr>
<th>Particle</th>
<th>Symbol</th>
<th>d\textsubscript{p} \textmu m*</th>
<th>Deposition by</th>
<th>Site of Deposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coarse</td>
<td>PM\textsubscript{10}</td>
<td>&gt;10</td>
<td>Wall impact</td>
<td>Conducting airways</td>
</tr>
<tr>
<td>Fine</td>
<td>PM\textsubscript{2.5}</td>
<td>10&gt;2.5</td>
<td>Combination†</td>
<td>Combination†</td>
</tr>
<tr>
<td>Ultrafine</td>
<td>PM\textsubscript{1.0}</td>
<td>&lt;0.1</td>
<td>Diffusion</td>
<td>Alveoli</td>
</tr>
</tbody>
</table>

* Aerodynamic diameter takes into account particle density and deviation of shape from a simple sphere. A high-density particle has a d\textsubscript{p} that is higher than its dm.
† Combined deposition by wall impact and sedimentation in conducting airways and respiratory bronchioles, respectively.

| TABLE 2. Increased Death Rate or Risk of Death in London Smog of 1952\textsuperscript{2} Compared With Data From Pope et al\textsuperscript{3} in Current Smokers and Never Smokers, 1982–1988 |
|-----------------|--------|-----------------|--------|
| Mortality From | Fold Increase in Death | 1982–1988\textsuperscript{3}: Relative Risk of Death |
| COPD | 9.5 | 9.85 | 0.84 |
| Pneumonia | 4.1 | 1.89 | 1.07 |
| Cardiovascular disease | 2.8 | 1.94 | 1.12 |
death from lung and cardiovascular disease. Such observations may provide evidence for or against an active role of long-term increases in air pollution on disease progression. It is here that the study provides the most interesting new information. By the elimination of the confounding issue of current and past smoking on mortality rate in Tables 4 and 5 of Pope et al., the overriding effect of smoking in the population at risk on mortality from air pollution becomes very clear. Eliminating smoking as a risk factor greatly reduces risk of death from both lung and cardiovascular disease, but this reduction is seen to a much greater extent in death from lung disease. The data also suggest that that a high incidence of smoking in the population at risk must have had a similar overriding effect on mortality from lung disease in many of the early short-term studies of air pollution disasters such as the London smog of 1952.

Conclusions
1. Chronically high levels of air pollution with fine and ultrafine suspended particulates constitute an important risk factor for progression of and death from cardiovascular disease in current smokers, past smokers, and never smokers.
2. Chronically high levels of air pollution appear not to be an important cause for increased risk of death from lung disease in never smokers, although this conclusion by Pope and his associates requires some reservations.
3. If the population at risk for high levels of chronic air pollution is made up of smokers, risk of death from lung disease is an order of magnitude greater than in a population of never smokers, whereas risk of death from cardiovascular disease is only about 50% to 70% higher. Thus, in a population of smokers, risk of death from lung disease becomes about 5 times higher than that from cardiovascular disease.
4. This explains why in much earlier studies of mortality from air pollution when incidence of smoking was very high, such as during the London smog of 1952, the risk of death from lung disease was very high (Table 2), but that from heart disease appeared insignificant.
5. These new findings should not be misinterpreted to indicate that high levels of air pollution have little or no effect on the lungs of never smokers. In never smokers, there is clear evidence that high levels of air pollution cause structural damage in the lung periphery and accelerate decline in lung function. Nonsmokers exposed to high levels of air pollution will probably not die of COPD, but they may develop a higher-than-normal risk of death from pneumonia or influenza consistent with the present data.

References

Key Words: Focused Perspectives ■ mortality ■ smoking ■ respiration ■ air pollution
Relative Effects of Air Pollution on Lungs and Heart
Robert L. Johnson, Jr

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