Ozone's impact on public health: Contributions from indoor exposures to ozone and products of ozone-initiated chemistry

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Many studies have reported associations between outdoor ozone concentrations and morbidity and mortality. Hubbell et al. (2005) systematically summarized this literature, including associations between ozone and respiratory-related hospital admissions, lost school days, restricted activity days, asthma-related emergency department visits, and premature mortality. Additionally, ozone has been associated with respiratory symptoms and the use of asthma medication for asthmatic school children using maintenance medication (Gent et al. 2003), and long-term exposure to ozone has been tentatively associated with the development of asthma in adult males (McDonnell et al. 1999). Since the submission of Hubbell et al. (2005), three independent meta-analyses have been published, indicating an increase of 0.87% in mortality per 10-ppb increase in daily ozone (Bell et al. 2005), an increase of 0.39% in mortality per 10-ppb increase in 1-hr daily maximum ozone (Ito et al. 2005), and an increase of 0.41% in mortality per 10-ppb increase in 1-hr daily maximum ozone (Levy et al. 2005); in most of the studies included in the meta analyses, same-day effects were larger than lagged effects. A study of 23 European cities found an increase of 0.66% in mortality per 10 ppb increase in 1-hr maximum ozone during the summer (Gryparis et al. 2004); a study in Genoa, Italy, found an increase of 0.60% in mortality per 25-ppb increase in ozone (Parodi et al. 2005); and a study in Shanghai found an increase of 0.45% in mortality per 5-ppb increase in 2-day average ozone (Zhang et al. 2006). Significantly, even when Bell et al. (2006) used data that included only days with average ozone levels lower than 15 ppb, outdoor ozone was significantly associated with premature mortality. For a more extended review of these and other studies, see the U.S. Environmental Protection Agency ozone criteria document (U.S. EPA 2006).

An increase in the concentration of outdoor ozone concomitantly produces an increase in the indoor concentrations of ozone and its reaction products (Weschler 2000). Thus, some of the associations between outdoor ozone and both morbidity and mortality are likely due to outdoor ozone transported into various indoor environments (e.g., residences, workplaces, schools, hospitals, motor vehicles) where subsequent exposures occur. Although indoor ozone concentrations tend to be smaller than corresponding outdoor concentrations, this is somewhat counterbalanced by the much larger fraction of time that most people spend indoors. Moreover, excepting nitrogen dioxide, total concentrations of ozone reaction products are anticipated to be larger indoors than outdoors (see “Products of ozone-initiated indoor chemistry”). My aim in this article is to present evidence supporting the hypothesis that indoor exposures to ozone and its oxidation products contribute to ozone’s overall impact on public health. Apportioning ozone’s health impact among indoor and outdoor ozone, as well as indoor and outdoor oxidation products, is more than an academic exercise. If indoor ozone and the products of its chemistry are adversely affecting the public’s health, relatively simple strategies can mitigate these effects.

**Indoor Ozone: Exposures and Intakes**

*Indoor ozone concentrations.* Although there are indoor sources of ozone, in most buildings indoor ozone has been transported from outdoors (Weschler 2000). Indoor ozone concentrations track outdoor concentrations with a slight time lag that depends on the air exchange rate. Ozone is removed by indoor surfaces as well as by gas-phase reactions, and hence, indoor concentrations tend to be smaller than co-occurring outdoor levels. Models have been presented that relate indoor ozone concentrations to those outdoors (Nazaroff and Cass 1986; Sabetsky et al. 1973; Shair and Heitner 1974). In the absence of indoor sources, the ratio of indoor to outdoor ozone concentrations (I/O) can be estimated using a relatively simple expression (Weschler et al. 1989):

$$I/O = \lambda/(\lambda + k_i),$$

where $\lambda$ is the air exchange rate and $k_i$ is the first-order rate constant for surface removal (both in units of reciprocal time). This equation assumes that the penetration coefficient for ozone is unity, an assumption that remains largely untested, and ignores gas-phase reactions.
reactions, which tend to be smaller sinks than surface reactions. Numerous investigators have measured surface removal rate constants for ozone, as summarized in several reviews (Grontofs and Raychoudhuri 2004; Nazaroff et al. 1993; Weschler 2000). For example, Lee et al. (1999) found a mean value of 2.8 ± 1.3 hr⁻¹ in 43 Southern California homes. A review of air exchange rates in residences and nonresidences has recently appeared in a draft U.S. EPA report (U.S. EPA 2005). Air exchange rates vary with the region and the season. In general, mean residential values are between 0.6 and 1.7 hr⁻¹, and mean nonresidential values are between 1.5 and 2.0 hr⁻¹. If a value of 3 hr⁻¹ is used for kᵫ, Equation 1 predicts an I:O of 0.10 at an air exchange rate of 0.33 hr⁻¹, an I:O of 0.33 at 1.5 hr⁻¹ and an I:O of 0.50 at 3 hr⁻¹. These calculated estimates are consistent with measured values, for example, a mean I:O of 0.37 ± 0.25 at 126 Southern California homes (Avol et al. 1998), and a mean I:O of 0.20 ± 0.18 at 145 homes in Mexico City and I:O values between 0.3 and 0.4 at three corresponding schools during class hours (Romieu et al. 1998); see table 2 of Weschler (2000) for a more extensive summary of measured I:Os for ozone.

Residences with central air conditioning (AC) have I:Os that are typically < 0.10 (Lee et al. 1999, 2004; Stock et al. 1985). This indicates an I:O of 0.10 at an air exchange rate of 0.95 m³/hr for children, 1.39 m³/hr for adults) were used for BRₑₐₑₑ, and breathing rates corresponding to sedentary activity (0.47 m³/hr for children, 0.54 m³/hr for adults) were used for BRₑₑₑₑ (U.S. EPA 1997).

Total breathing rates were used rather than fractional rates corresponding only to alveolar ventilation, because most of the inhaled ozone reacts with ascorbic acid, uric acid, glutathione, and unsaturated fatty acids present in the epithelial lining fluid in the conducting airways (Postlethwait and Ultman 2001; Rigas et al. 2000). Although outdoor ozone intakes in Figure 1B tend to be larger, indoor ozone intakes account for between 27 and 60% of total daily ozone intake and average just over 40%. Given that even low levels of ozone have been associated with increased risk of premature mortality (Bell et al. 2006), indoor intakes should not be ignored.

**Products of Ozone-Initiated Indoor Chemistry: Exposures and Intakes**

**Indoor sources of ozone-reactive chemicals.** Indoor exposure to ozone is accompanied by exposure to the products of ozone-initiated indoor chemistry (Weschler 2004). In general, these products are a consequence of ozone reacting with many commonly found organic chemicals that contain unsaturated carbon-carbon bonds (e.g., isoprene, styrene, terpenes,
Products of ozone-initiated indoor chemistry. There are several reasons why products of ozone-initiated chemistry tend to have higher concentrations indoors than outdoors. First, there are more ozone-reactive chemicals indoors than outdoors because of the presence of consumer products, architectural coatings, furnishings, and building materials; indeed, some sources occur almost exclusively indoors (e.g., carpets, linoleum, air fresheners). Second, concentrations of ozone-reactive compounds tend to be higher indoors than outdoors (Brown et al. 1994; Hodgson and Levin 2003; Wolkoff 1995), reflecting more sources and larger emission rates per volumetric flow rate. Third, surface-to-volume ratios (S:V) are roughly two orders of magnitude larger indoors than outdoors based on characteristic mixing heights outdoors (Nazaroff et al. 2003). This is partially counterbalanced by higher deposition velocities, \( v_d \), outdoors (Finlayson-Pitts and Pitts 2000) compared with indoors (Weschler 2000). On average, the first-order rate constant that describes surface removal (the product of S:V and \( v_d \)) is about 30 times larger indoors than outdoors. Indoor surface reactions are major sources of oxidation products (Destaillats et al. 2006b; Fick et al. 2004; Morrison and Nazaroff 2002; Weschler et al. 1992b; Wisthaler et al. 2005). Additionally, unlike gas-phase reactions (Weschler and Shields 2000), surface chemistry can include reactions whose rates are slower than air exchange rates.

Table 1. Indoor sources of reactive chemicals and common stable oxidation products resulting from ozone-initiated reactions with the specified emissions.

<table>
<thead>
<tr>
<th>Source</th>
<th>Reactive emissions</th>
<th>Major stable products</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupants (exhaled breath, skin oils, personal care products)</td>
<td>Isoprene, nitric oxide, squalene, unsaturated steroids, oleic acid and other unsaturated fatty acids, unsaturated oxidation products</td>
<td>Methacrolein, methyl vinyl ketone, nitrogen dioxide, acetylene, 8MHO, geranyl acetone, 40PA, formaldehyde, nonanal, decanal, 9-oxo-nonanoic acid, azelaic acid, nonanoic acid</td>
<td>Finlayson-Pitts and Pitts (2000), Frukelde et al. (1998), Thornberry and Abbatt (2004), Taucher et al. (1997), Wisthaler et al. (2005)</td>
</tr>
<tr>
<td>Soft woods; wood flooring including cypress, cedar, and silver fir boards; houseplants</td>
<td>Isoprene, limonene, ( \alpha )-pinene, other terpenes and sesquiterpenes</td>
<td>Formaldehyde, 4-AMC, pinonaldehyde, pinic acid, pinonic acid, formic acid, methacrolein, methyl vinyl ketone, SOAs including ultrafine particles</td>
<td>Aoki et al. (2005), Hodgson et al. (2000), Iwahishi et al. (2005), Kagi et al. (2005), Atkinson and Arey (2003), SOA references in text</td>
</tr>
<tr>
<td>Carpets and carpet backing</td>
<td>4-Phenylcyclohexene, 4-vinylcyclohexene, styrene, 2-ethylhexyl acrylate, unsaturated fatty acids and esters</td>
<td>Formaldehyde, acetaldehyde, benzaldehyde, hexanal, nonanal, 2-nonalen</td>
<td>Hodgson et al. (1993), Morrison and Nazaroff (2000, 2002), Weschler et al. (1992a)</td>
</tr>
<tr>
<td>Linoleum and paints/ polishes containing linseed oil</td>
<td>Linoleic acid, linolenic acid</td>
<td>Propanal, hexanal, nonanal, 2-heptenal, 2-nonalen, 2-decenal, 1-pentene-3-one, propanic acid, ( n )-butyric acid</td>
<td>Andersson et al. (1996), Clausen et al. (2005), Wolkoff (1995)</td>
</tr>
<tr>
<td>Latex paint</td>
<td>Residual monomers</td>
<td>Formaldehyde</td>
<td>Reiss et al. (1995a)</td>
</tr>
<tr>
<td>Certain cleaning products, polishes, waxes, air fresheners</td>
<td>Limonene, ( \alpha )-pinene, terpinolene, ( \alpha )-terpinene and other terpenes, ( \alpha )-terpinolene, linalool, linalyl acetate and other terpene aldehydes, longifolene and other sesquiterpenes</td>
<td>Formaldehyde, acetaldehyde, glycolaldehyde, formic acid, acetic acid, hydrogen and organic peroxides, acetone, benzaldehyde, 4-hydroxy-4-methyl-5-hexen-1-ol, 5-ethylidihydro-5-methyl-2(3H)-furanone, 4-AMC, SOAs including ultrafine particles</td>
<td>Aoki et al. (2005), Destaillets et al. (2006a), Englund et al. (1996), Liu et al. (2004), NAzaroff and Weschler (2004), Shu et al. (1997), Singer et al. (2006), Wolkoff et al. (1998), SOA references in text</td>
</tr>
<tr>
<td>Natural rubber adhesive</td>
<td>Isoprene, terpenes</td>
<td>Formaldehyde, methacrolein, methyl vinyl ketone</td>
<td>Aoki et al. (2005), Atkinson and Arey (2003)</td>
</tr>
<tr>
<td>Photocopy toner, printed paper, styrene polymers</td>
<td>Styrene</td>
<td>Formaldehyde, benzaldehyde, hexanal, glycoxl, ( N )-methylformamide, nicotinamide, acetone,</td>
<td>Aoki et al. (2005), Wolkoff et al. (1993), Wolkoff (1999)</td>
</tr>
<tr>
<td>Environmental tobacco smoke</td>
<td>Styrene, acrolein, nicotine</td>
<td>Formaldehyde, benzaldehyde, hexanal, glycoxl, ( N )-methylformamide, nicotinamide, acetone,</td>
<td>Destaillets et al. (2006b), Shaughnessy et al. (2001)</td>
</tr>
<tr>
<td>Soiled clothing, fabrics, bedding</td>
<td>Squalene, unsaturated steroids, oleic acid and other unsaturated fatty acids</td>
<td>Acetone, geranyl acetone, 8MHO, 40PA, formaldehyde, nonanal, decanal, 9-oxo-nonanoic acid, azelaic acid, nonanoic acid</td>
<td>Fruekilde et al. (1998), Thornberry and Abbatt (2004), Wisthaler et al. (2005)</td>
</tr>
<tr>
<td>Soiled particle filters</td>
<td>Unsaturated fatty acids from plant waxes, leaf litter, and other vegetative debris; seed; soil particles</td>
<td>Formaldehyde, nonanal, and other aldehydes; azelaic acid nonanoic acid; 9-oxo-nonanoic acid and other oxo-acids; compounds with mixed functional groups (=C=O, –OH, and –COOH)</td>
<td>Bekki et al. (2006), Hyttinen et al. (2003, 2006), Thornberry and Abbatt (2004)</td>
</tr>
<tr>
<td>Ventilation ducts and duct liners</td>
<td>Unsaturated fatty acids and esters, unsaturated oils, neoprene</td>
<td>( C_6 ) to ( C_{10} ) aldehydes</td>
<td>Morrison et al. (1998)</td>
</tr>
<tr>
<td>“Urban grime”</td>
<td>Polycyclic aromatic hydrocarbons</td>
<td>Oxidized polycyclic aromatic hydrocarbons</td>
<td>Kahan et al. (2006)</td>
</tr>
<tr>
<td>Perfumes, colognes, essential oils (e.g. lavender, eucalyptus, tea tree)</td>
<td>Limonene, ( \alpha )-pinene, pinonaldehyde, linalyl acetate, terpine-4-ol, ( \gamma )-terpinene</td>
<td>Formaldehyde, 4-AMC, acetone, 4-hydroxy-4-methyl-5-hexen-1-ol, 5-ethylidihydro-5-methyl-2(3H)-furanone, SOAs including ultrafine particles</td>
<td>Chao et al. (2005), Karamalegos et al. (2005), Shu et al. (1997), SOA references in text</td>
</tr>
<tr>
<td>Overall home emissions</td>
<td>Limonene, ( \alpha )-pinene, styrene</td>
<td>Formaldehyde, 4-AMC, pinonaldehyde, acetone, pinic acid, pinonic acid, formic acid, benzaldehyde, SOAs including ultrafine particles</td>
<td>Hodgson et al. (2000), Park and Ikeda (2006), Atkinson and Arey (2003), SOA references in text</td>
</tr>
</tbody>
</table>

Abbreviations: 4-AMC, 4-acyethyl-1-methyl-cyclohexene; 8MHO, 8-methyl-5-heptene-2-one; 40PA, 4-oxopentanal.
(Weschler et al. 1992a). These are highly reactive oxidants in their own right. Indeed, at typically anticipated indoor concentrations, ozone-derived nitrate radicals react much faster with alkenes and poly cyclic aromatic hydrocarbons (PAHs) than with ozone alone [see table 8 of Nazaroff and Weschler (2004)].

Secondary organic aerosols (SOAs), consisting of primarily fine and ultrafine particles, are an important subgroup of stable products resulting from ozone-initiated chemistry. They are formed from low-vapor pressure—oxidation products that partition between the gas phase and the surface of preexisting particles or nucleate to form new aerosols. The reaction of ozone with various terpenoids in indoor settings has been shown to contribute tens of micrograms per cubic meter to the indoor concentration of submicrometer particles under appropriate conditions (Destaillets et al. 2006a; Fan et al. 2003, 2005; Long et al. 2000; Rohr et al. 2003b; Sarwar et al. 2003, 2004; Wainman et al. 2000; Weschler and Shields 1999).

Studies indicating indoor exposure to SOAs from ozone-initiated chemistry. Particulate organic carbon was analyzed in samples of indoor and outdoor fine particles collected at 173 homes in Houston, Texas; Los Angeles, California; and Elizabeth, New Jersey. At least 40%, but more likely 70–75%, of the particulate organic carbon associated with indoor particles was generated indoors (Polidori et al. 2006). The authors speculated that a portion of this may have been contributions from SOAs generated by indoor ozone chemistry. Table 2 presents data from Sarnat et al. (2005) that support the concept that SOAs generated indoors can make meaningful contributions to personal exposures to particles < 2.5 µm in diameter (PM2.5). The table shows personal (P) and corresponding outdoor (O) concentrations of PM2.5 and fine-mode sulfate (SO42–) for senior citizens living in Boston, Massachusetts, during five monitoring periods. The fine-mode sulfate concentrations are derived from analyses of the PM2.5 filters and serve as markers for personal exposure to PM2.5 of outdoor origin because fine-mode sulfate has few indoor sources (Sarnat et al. 2002). Table 2 also shows personal-to-outdoor ratios (P:O) for PM2.5 and SO42–, as well as differences between these ratios [P:O (PM2.5) – P:O (SO42–)]. During winter 1 and winter 2, the difference between P:O (PM2.5) and P:O (SO42–) was approximately 0.35 (Table 2, next to last row). In contrast, during winter 3, summer 1, and summer 2, this difference was much larger, ranging from 0.75 to 1.55. The larger difference indicates that indoor sources were making a larger contribution to personal PM2.5 concentrations during these final three monitoring periods than during the first two monitoring periods. It is unlikely that this was due to recognized (Wallace et al. 2006) indoor sources of PM2.5 such as cooking, cleaning, and personal care because these sources should not be significantly stronger during milder weather. Nor is the larger difference due to more time indoors during the final three periods; the seniors were indoors 97% of the time in the winter and 93% of the time in the summer (time in transit included). Instead, the larger difference may be due to greater amounts of indoor ozone—generated SOAs during winter 3, summer 1, and summer 2 than during winter 1 and winter 2 [personal ozone concentrations (Table 2, last row) were 2.5, 5.1, and 4.8 ppb during the former periods and 0.1 and 0.8 ppb during the latter periods].

Additional data in Sarnat et al. (2005) lend further support to this interpretation. Regression results for measurements made during the summer months indicate a slope of 0.35 (0.22–0.47) for personal sulfate regressed on personal ozone, compared with a slope of 0.72 (0.42–1.01) for personal PM2.5 regressed personal ozone (see table 3 of Sarnat et al. 2005). The much larger slope for the latter pairing is consistent with contributions to personal PM2.5 from SOAs generated by ozone-initiated indoor chemistry.

Health effects of ozone reaction products. Certain ozone reaction products are known to have adverse health effects. For example, formaldehyde has been designated a Group 1 carcinogen in a 2004 International Agency for Research on Cancer evaluation (Cogliano et al. 2005). Acrolein is listed by California as an irritant and carcinogen (California Office of Environmental Health Hazard Assessment 2006). Peroxyacyl nitrate is a known eye irritant (Vyskocil et al. 1998), as are some of the products of ozone/terpene and ozone/isoprene chemistry (Kleno and Wolkoff 2004; Nojgaard et al. 2005). Hydroperoxides formed via the oxidation of terpenes and terpenoids can be potent contact allergens (Gaffet et al. 1994; Karlberg and DoomsGoossens 1997; Matusa et al. 2003, 2005; Skold et al. 2002). Leikauf (2002) has listed formaldehyde, acetaldehyde, and acrolein as compounds anticipated to induce or exacerbate asthma. Using a mouse model, Wolkoff and colleagues have demonstrated that ozone/terpene reactions produce strong airway irritants (Clausen et al. 2001; Rohr et al. 2002, 2003a; Wilkins et al. 2001; Wolkoff et al. 1999, 2000). However, an acute exposure study of healthy women exposed for 2 hr to a mixture of volatile organic compounds and ozone (40 ppb) did not result in significant subjective or objective symptoms (Fiedler et al. 2005; Laumbach et al. 2005), suggesting that longer exposures may be necessary to produce a measurable effect.

For some indoor oxidation products, the connection with adverse health effects is more tentative. For example, there is accumulating evidence that outdoor PM2.5 adversely affects morbidity and mortality (Dominici et al. 2006; Pope et al. 2002), and SOAs are major constituents of outdoor PM2.5. However, SOAs from ozone/terpenoid reactions differ in composition from SOAs generated by outdoor photochemical activity. It is not known how the toxicities of these SOAs compare. An additional consideration is the fact that ozone/terpenoid reactions lead to the co-occurrence of peroxides and submicrometer particles (Docherty et al. 2005; Fan et al. 2005; Li et al. 2002), and this may provide a mechanism to transport some of the peroxides deep into the respiratory tract (Friedlander and Yeh 1998). The consequences of inhaling such oxidation products, some of which are known contact allergens (see above), remain to be evaluated.

Hydroxyl and nitrate radicals, derived from ozone reactions, further react to produce still other oxidation products. Toxic products formed in this manner include malaoxon from the OH oxidation of malathion (Brown et al. 1993) and nitrosoamines and nitro-PAHs from reactions involving nitrate radicals (Gupta et al. 1996; Pitts et al. 1985).

Average daily indoor intakes of ozone reaction products. Ignoring gas-phase reactions, the ratio of the indoor concentration of ozone oxidation products to the indoor concentration of ozone, \[ \frac{[\text{Prod}]}{[O_3,\text{indo}]} = \left( \frac{F}{k_w} \right) / \lambda, \] is roughly estimated by

Table 2. Personal and outdoor concentrations (µg/m3) of PM2.5 and sulfate for senior citizens in Boston, as well as P:O ratios for each, the difference between these [P:O (PM2.5) – P:O (SO42–)], and the corresponding personal ozone concentrations (ppb).*

<table>
<thead>
<tr>
<th></th>
<th>Winter 1</th>
<th>Winter 2</th>
<th>Winter 3</th>
<th>Summer 1</th>
<th>Summer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal PM2.5</strong></td>
<td>10.8 (n = 40)</td>
<td>15.4 (n = 41)</td>
<td>18.2 (n = 51)</td>
<td>17.8 (n = 106)</td>
<td>20.5 (n = 59)</td>
</tr>
<tr>
<td><strong>Outdoor PM2.5</strong></td>
<td>13.1 (n = 13)</td>
<td>15.5 (n = 12)</td>
<td>6.5 (n = 15)</td>
<td>11.9 (n = 11)</td>
<td>13.1 (n = 13)</td>
</tr>
<tr>
<td>P:O (PM2.5)</td>
<td>0.82</td>
<td>0.99</td>
<td>2.49</td>
<td>1.50</td>
<td>1.54</td>
</tr>
<tr>
<td><strong>Personal SO42–</strong></td>
<td>1.6 (n = 51)</td>
<td>2.6 (n = 42)</td>
<td>1.6 (n = 56)</td>
<td>2.7 (n = 104)</td>
<td>3.3 (n = 59)</td>
</tr>
<tr>
<td><strong>Outdoor SO42–</strong></td>
<td>3.4 (n = 13)</td>
<td>4.2 (n = 12)</td>
<td>1.7 (n = 13)</td>
<td>3.6 (n = 8)</td>
<td>4.2 (n = 12)</td>
</tr>
<tr>
<td>P:O (SO42–)</td>
<td>0.47</td>
<td>0.62</td>
<td>0.94</td>
<td>0.75</td>
<td>0.79</td>
</tr>
<tr>
<td>P:O (PM2.5) – P:O (SO42–)</td>
<td>0.35</td>
<td>0.37</td>
<td>1.55</td>
<td>0.75</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>Personal O3</strong></td>
<td>0.1 (n = 50)</td>
<td>0.8 (n = 43)</td>
<td>2.5 (n = 57)</td>
<td>5.1 (n = 106)</td>
<td>4.8 (n = 50)</td>
</tr>
</tbody>
</table>

*Data from Sarnat et al. (2000, table 2).
where $k_e$ and $\lambda$ are as defined for Equation 1, and $F$ is the molar emission rate of oxidation products to ozone's surface removal rate (sometimes called the “formation factor”). Wisthaler et al. (2005) found that for every molecule of ozone removed by surfaces in a simulated aircraft cabin, between 0.2 and 0.25 molecules of oxidized products entered the air. For different types of carpets, Morrison and Nazaroff (2002, figure 5) report that for each ozone molecule removed, 0.1–0.7 aldehyde molecules entered the air. For four different types of surfaces in four different homes, Wang and Morrison (2006) report that for each ozone molecule removed, 0.1–0.4 aldehyde molecules entered the air. In the latter two studies, the total number of oxidized molecules that entered the air is presumed larger than that reported for aldehydes alone because common oxidation products such as formic acid, acetic acid, and acetone were not included in the aldehyde numbers. Although more measurements of $F$ are needed in residences and nonresidences, these studies are a beginning. Using a middle estimate of 0.33 for $F$ and combining it with a value of 3 hr$^{-1}$ for $k_e$ and a range of values from 0.5 to 3 hr$^{-1}$ for $\lambda$, a conservative estimate for $[\text{Prod}]_{\text{O}_3,\text{ind}}$ is 0.33–2. This estimate is termed “conservative” because it considers only airborne products derived from surface chemistry; additional oxidation products derived from gas-phase chemistry (e.g., ozone reacting with terpenes) would result in a larger ratio. Hence, it is reasonable to anticipate that ozone oxidation products are present indoors at concentrations that, on a molar basis, are roughly one-third to twice those of ozone alone. This means that average daily indoor intakes of ozone oxidation products are roughly one-third to twice that of ozone (Figure 1B). Because the products of ozone-initiated chemistry tend to have higher concentrations indoors than outdoors (see above) and that greater time spent indoors overwhelms larger breathing rates outdoors, indoor inhalation intakes of oxidation products tend to be much larger than outdoor intakes of oxidation products.

In a region with moderate outdoor ozone levels, persons doing their own day-to-day house cleaning are estimated to inhale an average of 20 µg/day of formaldehyde and 35 µg/day of SOAs (a large fraction of which are ultrafine particles) as a consequence of ozone-initiated reactions with constituents of cleaning agents and air fresheners [table 5.3 of Nazaroff et al. (2006)]. These values are consistent with intakes of oxidation products estimated in the previous paragraph. Such inhalation intakes add to already existing and often significant intakes of formaldehyde and SOAs from other sources. Furthermore, reactions between ozone and constituents of personal-use products (e.g., perfumes, colognes, hair treatments) emit oxidation products in the vicinity of the breathing zone, resulting in inhalation intakes larger than those predicted if the products were evenly distributed throughout a room (Karamalegos et al. 2005).

### Connections Between III Health and Exposure to Indoor Ozone and Its Oxidation Products

**Recent epidemiologic study of mortality in 95 U.S. urban communities.** Bell et al. (2004) have used databases from the National Morbidity, Mortality and Air Pollution Study to calculate the average relative rate of mortality associated with short-term ozone concentrations measured at outdoor monitoring stations for 95 U.S. cities between 1987 and 2000. Table 3 presents the 10 cities with the highest percent change in daily mortality per 10-ppb increase in daily ozone and the 10 cities with the lowest percent change. For each of the listed cities, Table 3 also presents the percentage of population growth for the period 1990–2000 and the percentage of residences with central AC. The data were obtained from the U.S. Census Bureau (2006); for selected cities where specific information on central AC was not available, the value is simply listed as being greater than or less than 70% on the basis of comparisons with cities that have similar seasonal dew points and temperatures.

Cities with recent population growth have a larger fraction of new homes and apartments than cities with less growth, and such newer residences tend to have lower air exchange rates (Weisel et al. 2005). Use of central AC is also associated with low air exchange rates (see “Indoor ozone concentrations” above). Conversely, without AC, residents are more likely to open their windows during periods when temperatures are elevated. Hence, compared with older cities that have fewer homes with central AC, newer cities with a higher prevalence of central AC are anticipated to have less outdoor-to-indoor transport and smaller occupant exposures to indoor ozone and the products of ozone-initiated chemistry. Consistent with a connection between such indoor exposures and mortality, 8 of the 10 cities that had the highest percent increase in mortality per 10-ppb increase in ozone had population growth since 1990 > 10% and 8 of the 10 had central AC in < 70% of the structures, whereas 7 of the 10 cities that had the lowest percent increase in mortality per 10-ppb increase in ozone had population growth since 1990 > 10% and 7 of the 10 had central AC in > 70% of its structures (Table 3).

**Other suggestive studies.** Levy et al. (2005) conducted an empiric Bayes meta regression to examine the relationship between outdoor ozone concentrations and premature mortality based on 48 estimates from 28 time-series studies. The authors deliberately omitted data from the National Morbidity, Mortality and Air Pollution Study (2006) because other investigators were analyzing these data. In other words, their database was independent of data that are the basis for Table 3. One of the conclusions from their meta regression was

<table>
<thead>
<tr>
<th>Ten cities with highest percent change of 95 cities</th>
<th>Change in daily mortality (%)</th>
<th>Population growth, 1990–2000 (%)</th>
<th>Central AC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York City</td>
<td>1.7</td>
<td>9.4</td>
<td>16</td>
</tr>
<tr>
<td>Newark, NY</td>
<td>1.3</td>
<td>-0.6</td>
<td>47</td>
</tr>
<tr>
<td>Philadelphia, PA</td>
<td>1.3</td>
<td>-4.3</td>
<td>50</td>
</tr>
<tr>
<td>Cincinnati, OH</td>
<td>1.2</td>
<td>-8.0</td>
<td>66</td>
</tr>
<tr>
<td>Dallas/Ft. Worth, TX</td>
<td>1.1</td>
<td>18.6</td>
<td>91</td>
</tr>
<tr>
<td>Shreveport, LA</td>
<td>1.0</td>
<td>0.8</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>Chicago, IL</td>
<td>0.9</td>
<td>4.0</td>
<td>62</td>
</tr>
<tr>
<td>Syracuse, NY</td>
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<td>-10.1</td>
<td>&lt; 70</td>
</tr>
<tr>
<td>Colorado Springs, CO</td>
<td>0.9</td>
<td>28.4</td>
<td>&lt; 70</td>
</tr>
<tr>
<td>Worcester, MA</td>
<td>0.9</td>
<td>1.7</td>
<td>&lt; 70</td>
</tr>
<tr>
<td>Average</td>
<td>1.1</td>
<td>3.9</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ten cities with lowest percent change of 95 cities</th>
<th>Change in daily mortality (%)</th>
<th>Population growth, 1990–2000 (%)</th>
<th>Central AC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlando, FL</td>
<td>-0.2</td>
<td>12.9</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>Denver, CO</td>
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<td>18.6</td>
<td>50</td>
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<tr>
<td>San Antonio, TX</td>
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<td>22.3</td>
<td>78</td>
</tr>
<tr>
<td>Las Vegas, NV</td>
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<td>85.2</td>
<td>&gt; 70</td>
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<td>Little Rock, AR</td>
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<td>4.2</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>Lexington, KY</td>
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<td>15.6</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>Birmingham, AL</td>
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<td>77</td>
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<tr>
<td>San Diego, CA</td>
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<td>10.2</td>
<td>34</td>
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<tr>
<td>St. Petersburg, FL</td>
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<tr>
<td>Lafayette, IN</td>
<td>0.3</td>
<td>28.9</td>
<td>&lt; 70</td>
</tr>
<tr>
<td>Average</td>
<td>0.1</td>
<td>20.0</td>
<td></td>
</tr>
</tbody>
</table>

*–, negative value.

Data from Bell et al. (2004). Data from U.S. Census Bureau (2006).
that AC prevalence was among the strongest predictors of between-study variability. They go on to state that their results suggest “that the ambient ozone-mortality relationship might be lower in cities with greater prevalence of residential central air conditioning (and therefore lower personal exposure to zone).”

Time-series epidemiologic studies often show seasonal differences in the relative risk from ozone (Ito et al. 2005; Levy et al. 2005; Wong et al. 2001; Zhang et al. 2006). Ozone risk estimates are larger for summer than for winter in New York City; Detroit, Michigan; and Cook County, Illinois (Ito et al. 2005). Conversely, ozone risk estimates are larger for winter than for summer in Houston (Ito et al. 2005), Hong Kong (Wong et al. 2001), and Shanghai (Zhang et al. 2006). In New York, Detroit, and Cook County, there is less outdoor-to-indoor transport during the cold winter, when windows tend to be closed, compared with the warmer summer. Indeed, in Boston, a climatically similar urban area, the association between outdoor ozone and personal ozone has been shown to be weaker in winter than in summer (Sarnat et al. 2005). However, in a southern city such as Houston or a subropical Asian city such as Hong Kong or Shanghai, there is less outdoor-to-indoor transport during the hot, humid summer, when air conditioners are used extensively and buildings tend to be sealed, compared with the cooler winter when buildings tend to be more open.

**Conclusions**

Indoor ozone and products of ozone-initiated indoor chemistry correlate with ozone measured at fixed outdoor sites. I have cited studies indicating that a) indoor ozone levels are typically 10–50% of outdoor values, b) indoor ozone exposures are typically 45–75% of total exposures, c) indoor ozone inhalation intakes are typically 25–60% of total intakes, d) indoor sources of chemicals that react with ozone are ubiquitous, e) certain oxidation products are known to be toxic and others are anticipated to be toxic, and f) indoor inhalation intakes of these oxidation products are roughly one-third to twice the indoor intakes of ozone and much greater than outdoor intakes of oxidation products. Smaller indoor intakes of ozone are anticipated for people who spend a large fraction of their time in indoor air-conditioned rooms or in rooms with small air exchange rates during periods when outdoor ozone levels are elevated. Smaller indoor intakes of oxidation products are anticipated for people who live in indoor settings with relatively low concentrations of ozone-reactive chemicals, both in the gas phase and associated with surfaces; smaller indoor intakes of oxidation products also result from higher air exchange rates (Equation 4).

By their nature the cited epidemiologic studies include the indoor exposures discussed in this article. Findings from several epidemiologic studies hint at associations between morbidity and mortality and indoor ozone and its oxidation products. However, these studies were not designed to test this hypothesis. Specific studies can be envisioned to evaluate the contribution of indoor ozone and its oxidation products to ill health (Weschler 2004).

Appportioning risk between outdoor and indoor intakes bears on the strategies used to protect public health. Outdoor ozone is harmful to health; outdoor ozone transported indoors is harmful to health; indoor ozone reacts to form products that are also harmful to health, some perhaps more so than ozone. Contrary to popular wisdom, being indoors does not offer clear protection from ozone-related adverse health effects, but it would if ozone were deliberately removed from ventilation air.

Although it has proven difficult and very costly to reduce outdoor ozone concentrations, relatively simple steps can reduce the concentration of indoor ozone and its oxidation products. For example, charcoal filters (Shair 1981; Shields et al. 1999) or chemically impregnated filters (Kelly and Kinkead 1993) could remove a large fraction of ozone in buildings with mechanical ventilation systems. In naturally ventilated buildings, strategies could be employed that reduce ventilation for the portion of the day when ozone is elevated and increase ventilation when ozone levels are lower. The use of products with ozone-reacting constituents could be limited during periods when indoor ozone levels are elevated. Such steps might be especially valuable interventions in schools, hospitals, and childcare centers in regions that continue to experience elevated outdoor ozone concentrations.

**References**


Exposure to indoor ozone and its reaction products

Contact allergy to resin acid hydroperoxides—haptens binding via free-radicals and epoxides. Chem Res Toxical 7(2):260–266.


Nazaroff WW, Weschler CJ. 2004. Cleaning products and air fresheners: exposure to primary and secondary air pollu-


1997. Detection of isoprene in expired air from human sub-
Thornberry T, Abbatt JPD. 2004. Heterogeneous reaction of ozone
with liquid unsaturated fatty acids: detailed kinetics and gas-
U.S. Census Bureau. 2006. American FactFinder and American
home/saffmain.html?_lang=en [accessed 22 March 2006].
Washington, DC. U.S. Environmental Protection Agency, Of-
epa.gov/ncea/pdfs/efh/ [accessed 22 March 2006].
Environmental Protection Agency, Office of Air Quality
ttnnaaqs/standards/ozone/data/O3-exposure-draft-TSD.pdf
[accessed 30 May 2006].
U.S. EPA. 2006. Air Quality Criteria for Ozone and Related
Photochemical Oxidants (Final). EPA/600/R-05/004f-cF.
Washington, DC. U.S. Environmental Protection Agency.
limonene in indoor air: a source of submicron particle expo-
Wallace L, Williams R, Rea A, Croghan C. 2006. Continuous week-
long measurements of personal exposures and indoor con-
centrations of fine particles for 37 health-impaired North
Carolina residents for up to four seasons. Atmos Environ
Wang H, Morrison GC. 2006. Ozone initiated secondary emission
2006].
2005. Relationships of Indoor, Outdoor, and Personal Air
(RIOPA): Part 1. Collection Methods and Descriptive
Weschler CJ. 2000. Ozone in indoor environments: concentration
products indoors may be more harmful than ozone itself.
Weschler CJ, Brauer M, Koutrakis P. 1992a. Indoor ozone and
nitrogen-dioxide—a potential pathway to the generation of
nitrate radicals, dinitrogen pentaoxide, and nitric-acid
Weschler CJ, Hodgson AT, Wooley JD. 1992b. Indoor chemistry
—ozone, volatile organic-compounds, and carpets. Environ
Weschler CJ, Shields HC. 1996. Production of the hydroxyl radical
Weschler CJ, Shields HC. 1999. Indoor ozone/terpene reac-
tions as a source of indoor particles. Atmos Environ
Weschler CJ, Shields HC. 2000. The influence of ventilation on
reactions among indoor pollutants: modeling and experi-
Wilkins CK, Clausen PA, Wilkoff P, Larsen ST, Hammer M,
Larsen K, et al. 2001. Formation of strong airway irritants in
mixtures of isoprene/ozone and isoprene/ozone/nitrogen
Withshaler A, Tamas G, Wyon DP, Strom-Tejsen P, Space D,
Beauchamp J, et al. 2005. Products of ozone-initiated chem-
istry in a simulated aircraft environment. Environ Sci Technol
Wolkoff P. 1995. Volatile organic compounds—sources, measure-
ments, emissions, and the impact on indoor air quality.
Indoor Air Suppl 3:9–73.
Wolkoff P. 1999. Photocopiers and indoor air pollution. Atmos
Wolkoff P, Clausen PA, Wilkoff CK, Hougaard KS, Nielsen GD.
1999. Formation of strong airway irritants in a model mixture
of strong airway irritants in terpene/ozone mixtures. Indoor
Air 10(2):82–91.
on daily mortality in Hong Kong. Environ Health Perspect
Zhang J, Liow P.J. 1994. Ozone in residential air—concentrations,
I/O ratios, indoor chemistry, and exposures. Indoor Air
indoor air: a field study. J Expo Anal Environ Epidemiol
4:25–47.
Ozone and daily mortality in Shanghai, China. Environ Health
Perspect 111:1227–1232.
Ziemann PJ. 2003. Formation of alkoxyhydroperoxy aldehydes
and cyclic peroxyhemiacetals from reactions of cyclic alk-
ones with O₃ in the presence of alcohols. J Phys Chem A
107(12):2048–2060.