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Environmental and occupational health was a major focus of both the scientific and lay press in 2009. Population-based studies confirmed the importance of environmental pollutants in the development of cardiorespiratory morbidity and mortality. Concerns regarding climate change highlighted the important public health consequences of carbon dioxide and methane emissions. The promise of new manufactured nanomaterials has been tempered by emerging concerns regarding their environmental impact. In addition, a ruling by the U.S. Supreme Court in 2009 will force a revision of the U.S. Environmental Protection Agency (EPA) standards for the three major air pollutants, particulate matter, ozone, and nitrogen oxides (NOx), in 2010. In this review on environmental and occupational medicine, we provide an overview of studies in the *American Journal of Respiratory and Critical Care Medicine* and selected other studies from the literature focused on environmental and occupational health. Although by no means comprehensive, we attempt to highlight the progress that has been made in identifying major health consequences of environmental exposure and understanding the mechanisms by which these occur.

CARDIORESPIRATORY EFFECTS OF AIR POLLUTION

Studies in Human Populations or Subjects

The relationship between air pollution and both respiratory and cardiovascular disease has been established, but many details about this relationship remain incompletely defined. The year 2009 saw the publication of several epidemiological studies that begin to fill in important details about the mechanisms responsible for the impacts of air pollution, the role of specific individual pollutants and pollutant components, threshold and dose–response effects, and the impact of improvement in pollution concentrations on human health.

New proposed standards for air pollutants. Since the passage of the Clean Air Act, epidemiological, controlled human exposure, and animal toxicological studies have played a role in helping to determine the U.S. National Ambient Air Quality Standards (NAAQS), which set limits for criteria air pollutants on the basis of expected health impacts. In 2009, anticipating an EPA proposal on the primary nitrogen dioxide (NO_2) standard, the American Thoracic Society Environmental Policy Committee recommended addition of a new short-term NO_2 NAAQS to the existing annual average standard (1). This decision sprang from studies, over more than a decade, suggesting acute health effects of NO_2 at levels below the current NAAQS standard, particularly in sensitive subpopulations during short-term peaks. Adding to this evidence, a cohort study demonstrated significant health effects at concentrations much lower than the NAAQS in 2009. This Toronto-based study consisting of respiratory clinic patients demonstrated significant increases in mortality (a 17% increase in all-cause and a 40% increase in circulatory mortality) associated with small (4 ppb) long-term increases in NO_2 in a region with annual average NO_2 concentrations in the range of 20–25 ppb (2). In June 2009, the EPA proposed a new 1-hour standard for NO_2 of 80–100 ppb while maintaining the existing annual average standard.

Similar to NO_2, studies in 2009 continued to call into question the adequacy of the current ozone limits. A controlled human exposure study of 31 young healthy adults showed that short-term ozone concentrations below the NAAQS induce significant changes in FEV_1 and respiratory symptoms (3). In an American Cancer Society cohort study, long-term ozone exposures were associated with respiratory but not cardiovascular mortality at concentrations lower than the current NAAQS, even after adjustment for fine particulate matter air pollution ($PM_{2.5}$, i.e., particles 2.5 μm in diameter and smaller) (4). Since then, the EPA has proposed (January 2010) a more protective NAAQS for ozone (changing the standard from 75 to 60–70 ppb).

The particulate matter–mortality dose–response curve. If one assumes a linear relationship between risk of cardiovascular mortality and particulate matter exposure, the risks of ambient air pollution–related death seen in cohort studies have appeared unexpectedly large compared with the risks of death from cigarette smoking. Given that the ambient PM NAAQS are based largely on the results of ambient air pollution cohort studies, a more detailed understanding of the shape of the dose–response relationship has been needed. In a study of more than 1 million adults also in the American Cancer Society cohort, Pope and colleagues estimated the dose–response curve for fine particles, using individual-level data on $PM_{2.5}$ exposures, cigarette smoking, potential confounders, and death certificates (5). This study demonstrated what appears to be a log-linear dose–response relationship between particles and mortality, with a much steeper dose response at relatively low ambient levels than at cigarette-smoking exposure levels. This study adds to evidence suggesting that even low-level PM exposures (both as

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ambient and second-hand smoke exposures) have important public health consequences, given the steep slope of the exposure response relationship at typical U.S. ambient levels.

Increased life expectancy, decreased respiratory symptoms related to reductions in PM. Given increasing evidence that air pollution has short- and long-term health effects, whether reductions in pollutant levels result in improvements in health outcomes has gained attention as air pollutant standards are evaluated for public health impacts. A large ecological study examining the relationship between changes in mortality and changes in air pollution levels across 211 U.S. counties demonstrated significant improvements in life expectancy related to reductions in $PM_{2.5}$ concentrations (6). Although this study was ecological in design and had limited direct information about potential confounders, it was the first population-based study to directly demonstrate improvements in life expectancy related to decreases in pollutant concentrations.

Several other efforts in 2009 demonstrated improved respiratory health outcomes related to reductions in air pollution levels. A cohort study of Swiss adults demonstrated that decreases in ambient PM_{10} are associated with reduced respiratory symptoms (7). A randomized trial of properly vented wood-burning cook stoves versus open fires in rural Mexico showed significant reductions in longitudinal FEV_1 decline and improved respiratory symptoms with adherence to the cook stove intervention (8). Similar effects on respiratory symptoms but not FEV_1 were found in a comparable Guatemalan cook stove study (9).

Clarifying the mechanisms responsible for the health effects of air pollution. In an effort to understand the mechanisms responsible for the detrimental effects of air pollution, several investigations in 2009 identified potentially important genetic pathways. In the VA Normative Aging Study, $PM_{2.5}$ was associated with postural changes in blood pressure, an effect that was modified by single-nucleotide polymorphisms (SNPs) in genes potentially involved in the development of chronic obstructive pulmonary disease (COPD) or asthma (*PHF11*, *MMP1*, and *ITPR2*) (10). Traffic-related black carbon particles but not $PM_{2.5}$ were associated with blood pressure in the same cohort, an effect that was not modified by SNPs or variants in oxidative defense genes (*GSTM1*, *GSTP1*, *GSTT1*, *NQO1*, *CAT*, or *HMOX-1*) (11). In myocardial infarction survivors from five European cities, SNPs in fibrinogen genes (*FGA* and *FGB*) modified the observed impact of PM_{10} on fibrinogen levels (12). Another study in this European cohort showed modification of the effect of carbon monoxide on IL-6 levels by polymorphisms in IL-6 and fibrinogen (13). Results from a Swiss cohort study in which decreased PM_{10} was associated with reduced age-related lung function decline suggested that SNPs in genes involved in cell cycle control (*p53*, *p21*, and *CCND1*) might modify these effects (14).

Relative toxicity of air pollution components and size fractions. Although ambient particles and gases have been associated with cardiorespiratory disease, the responsible size fraction or composition of particles and the pollutant-specific health effects remain poorly understood. Several studies in 2009 demonstrated that traffic-related pollutants, and specific components of PM, might be responsible for many of the health effects of air pollution.

In one of a few studies to specifically address the chemical composition of $PM_{2.5}$ responsible for its effect on disease, Bell and colleagues conducted a 106 U.S. county study of the relationship between long-term average $PM_{2.5}$ composition and risk of same-day hospitalizations for cardiorespiratory symptoms (15). Higher $PM_{2.5}$ fractions of nickel, vanadium, and elemental carbon showed the largest increases in hospitalizations compared with other components, a finding that may explain previously observed regional variations in particle-related health impacts. Examining respiratory symptoms in a different population (children less than 2 yr of age), Patel and colleagues also found that nickel, vanadium, and elemental carbon showed the largest effects (16). A study based on Medicare claims data for 12 million enrollees in 119 U.S. urban areas assessed the relationship between respiratory and cardiovascular hospitalizations and $PM_{2.5}$ components including sulfate, nitrate, silicon, elemental carbon (EC), organic carbon matter (OCM), and sodium and ammonium ions. In this study, the largest risks of hospitalization were associated with EC and OCM (17). Similarly, a panel study demonstrated effects of traffic-related components EC, OC, CO, and NOx on biomarkers of systemic inflammation, platelet activation, and erythrocyte antioxidant activity (18). An investigation that used Medicare data to evaluate the effect of carbon monoxide on cardiovascular hospitalizations demonstrated significant effects of carbon monoxide, independent of other copollutants, at levels below current NAAQS (19).

Several studies noted similar health effect magnitudes for various particle sizes (ultrafine [$PM_{0.1}$] vs. fine [$PM_{2.5}$] vs. coarse [$PM_{10-2.5}$] fractions). These studies were not primarily designed to directly compare the effects of particle size fractions, and each had different designs: controlled human trials of ultrafine particle exposure and heart rate variability (20), coarse particle exposure and lung inflammation (21) and a multicity study using National Center for Health Statistics data to examine the relationship between coarse particle exposure and daily mortality (22).

Novel health effects of air pollutants. As described previously, most air pollution epidemiological research in 2009 focused on the impact of air pollution on outcomes such as respiratory (or cardiovascular) hospitalizations or deaths, respiratory health, and biomarkers of inflammation (23) and hemostasis (24). Traffic-related air pollution in particular was also associated with several novel or less-studied outcomes in 2009, including deep venous thrombosis (25), DNA methylation (26), telomere shortening (27), left ventricular mass (28), and infant bronchiolitis (29).

Acute effects of secondhand smoke. Adding to a large and growing body of research documenting the chronic health impacts of secondhand smoke, a well-designed randomized human cross-over study demonstrated rapid (1 h) acute changes in inflammatory biomarkers and measures of lung function associated with secondhand smoke (30).

Mechanistic Studies in Animals or Cell-based Systems

Outdoor air pollution. CARDIOVASCULAR EFFECTS OF AMBIENT PARTICULATE MATTER. There have been several animal studies that have evaluated the contribution of ambient particulate matter (PM) air pollution to the cardiovascular disease seen in humans. Diesel exhaust (DE), a major component of near-road and ambient PM, has consistently shown cardiovascular impairment in clinical and experimental studies. Gottipolu and colleagues reported that subacute (4 wk) exposure to DE enhanced cardiac mitochondrial oxidative stress in both healthy and spontaneously hypertensive rats and produced a gene expression pattern associated with mitochondrial oxidative stress in the ventricles of healthy rats (31). In dogs exposed to concentrated ambient particles, Bartoli and colleagues observed an increase in systolic and diastolic blood pressure and heart rate associated with an increase in baroreceptor reflex sensitivity (32). Coronary artery occlusion in this model was associated with a reduction in myocardial blood flow and an increase in coronary vascular resistance (33). Similar to the effects of DE and ambient PM, short-term (1–48 h) exposure to residual oil fly ash, an emission source particle rich in transition metals, caused the development of nonconducted P-wave arrhythmias in spontaneously hypertensive rats (34). Collectively, these studies suggest that ambient

particle exposure might increase the propensity toward adverse cardiovascular outcomes through activation of the sympathetic nervous system.

In 2009, several groups sought to examine the mechanisms linking ambient particulate matter exposure and cardiovascular effects. Several groups explored the observed link between air pollution and the progression of atherosclerosis. In apolipoprotein E–null ($ApoE^{-/-}$) mice, Campen and colleagues simultaneously showed that exposure to DE resulted in dose-related alterations in gene markers of vascular remodeling and aortic lipid peroxidation in mice receiving a high-fat diet (35). As filtration of the PM did not significantly alter these vascular responses, they concluded that the gaseous portion of the exhaust was a principal driver (35). In a concentrated ambient particle exposure study using $ApoE^{-/-}$ mice, Ying and colleagues found that ambient PM enhances atherosclerosis through the NAD(P)H oxidase–dependent induction of vascular reactive oxygen species (ROS) and reactive nitrogen species, causing decreased guanine cyclase–dependent arterial constriction in response to phenylephrine (36). The same group of investigators reported that $PM_{2.5}$ causes activation of the Rho–Rho kinase pathway in aorta and myocardium, promoting cardiac fibrosis in mice (37).

Sun and colleagues evaluated the link between pollution and type 2 diabetes mellitus, a major risk factor for atherosclerosis and ischemic cardiovascular disease (38). Mice fed a high-fat diet for 10 weeks and then exposed to $PM_{2.5}$ for 24 weeks developed insulin resistance, systemic inflammation, and increased visceral adiposity compared with mice exposed to filtered air. These changes were associated with decreased Akt and nitric oxide synthase phosphorylation in the endothelium as well as increased cell adhesion in the microcirculation and the accumulation of monocytes in the visceral fat.

Further evidence was provided suggesting that PM-induced changes in vascular reactivity or pulmonary inflammation might contribute to the cardiovascular mortality associated with PM exposure. Cherng and colleagues reported that $PM_{2.5}$ exposure increased vascular endothelin-1 production. Acute exposure to DE altered endothelin-dependent vasoconstriction (39). Miller and colleagues offered an intriguing explanation for the reduction in NO-dependent vasorelaxation observed in PM-exposed animals. They reported that PM-induced oxygen-centered free radicals, such as superoxide, were produced at sufficient levels to oxidize endogenous NO (40). In a follow-up to their report showing that lung inflammation was required for the development of a prothrombotic state in PM-exposed mice, Urich and colleagues (41) and Soberanes and colleagues (42) linked mitochondrially derived ROS and Noxa (a proapoptotic Bcl-2 protein)–dependent epithelial cell death with PM-induced inflammation in the lung.

AIR POLLUTION AND AIRWAY DISEASE. Ambient PM is associated with exacerbations of asthma and can act as an adjuvant for allergic sensitization. Redox-active organic chemicals on the particle surface may determine the adjuvant effect of various particle types according to their potential to perturb redox equilibrium in the immune system. In a murine model of allergic sensitization, Li and colleagues reported that ambient ultrafine particles (UFPs) (aerodynamic diameter, <0.15 μm), but not fine particles (diameter, <2.5 μm), can act as an adjuvants to promote helper T-cell type 2 polarization and to enhance allergic sensitization (43). The adjuvant effect of the UFPs was closely related to the prooxidative organic chemical content on these particles. In a subsequent article from the same group, proteomic evaluation showed that polymeric immunoglobulin receptor, complement C3, neutrophil gelatinase–associated lipocalin, chitinase 3–like protein-3, chitinase 3–like protein-4, and acidic mammalian chitinase were significantly up-regulated by UFPs with a higher polycyclic aromatic hydrocarbon content and a higher oxidant potential (44). These results suggest that these proteins may be the important specific elements targeted by PM in air pollution through the ability to generate ROS in the immune system, and may be involved in allergen sensitization and asthma pathogenesis.

Other studies explored potential mechanisms linking PM exposure with the development of inflammation. Li and colleagues have shown that DE particles can activate the *MMP1* gene in normal human bronchial epithelial cells via Ras and subsequent activation of Raf–MEK (mitogen-activated protein kinase [MAPK]/ERK [extracellular signal–regulated kinase])–ERK1/2 mitogen–activated protein kinase signaling, which can be scaffolded by β-arrestins (45). They also found that transcriptional regulation of the human *MMP1* promoter was strongly influenced by the presence of the −1607 GG polymorphism, present in 60–80% of humans. In peritoneal macrophages from knockout mice, Schoenfelt and colleagues found that coarse and fine particles differentially engaged Toll-like receptor-2 (TLR2) and TLR4, respectively, to activate a key adaptor protein, MyD88, and induce the expression of proinflammatory cytokines (46).

RELATIVE TOXICITY OF AIR POLLUTION COMPONENTS AND SIZE FRACTIONS *IN VITRO*. Investigators evaluating the ability of various constituents of the ambient PM to induce an inflammatory response *in vitro* found that photooxidized organic compounds together with transition metals (nickel and vanadium) originating from fuel combustion made the greatest contribution to the inflammatory activity of fine particles in macrophages (RAW 246.7 cells) (47). Polycyclic aromatic hydrocarbons from incomplete biomass and coal combustion were primarily associated with cytotoxicity. Cho and colleagues found differential cardiac and pulmonary toxicity associated with PM on the basis of size (ultrafine, <0.1 μm; fine, 0.1–2.5 μm; coarse, 2.5–10 μm) and distance from an interstate highway in Raleigh, North Carolina (48). On a comparative mass basis, the coarse and ultrafine PM affected the lung and heart, respectively. Stoeger and colleagues evaluated whether the *in vivo* toxicity of combustion-derived nanoparticles could be predicted *in vitro* by a cell-free ascorbate test evaluating the oxidative potency of particles (49). In the six different types of combustion-derived nanoparticles examined, organic content–specific Brunauer, Emmett, and Teller (BET) surface area strongly correlated with the *in vivo* inflammatory response.

Indoor air pollution. Biomass smoke is an important source of PM with serious human health effects. Chronic lower levels of exposure can be overlooked and hence there is a need for the development of biomarkers to evaluate for exposure to biomass smoke. Migliaccio and colleagues reported that levoglucosan (1,6-anhydro-β-D-glucopyranose), a sugar anhydride released by combustion of cellulose-containing materials, can be recovered from the urine of mice within 4 hours of exposure and from healthy children exposed to wood smoke (50). Yoshida and colleagues investigated the effect of 2-ethyl-hexanol (2-EH), a known indoor air pollutant, on immune cells *in vitro* and reported that 2-EH is capable of activating $CD4^+$ cells with no effect on $CD8^+$ cells, suggesting that 2-EH could function as a modulator of immune response and may play a role in the pathogenesis of indoor pollution–induced asthma exacerbations (51). Organic dust exposure in agricultural animal environments results in airway diseases and dendritic cells (DCs) are likely to play an important role in this response. Poole and colleagues reported that exposure to organic dust during early monocyte differentiation can potentially impact the critical balance of DCs in the lung by altering the differentiation of monocytes to

immature DCs and the maturation of immature DCs into mature DCs (52).

Ozone. Several groups sought to determine the mechanisms by which ozone induces inflammation and airway hyperresponsiveness (AHR). The importance of oxidant stress in ozone-induced injury was confirmed in several studies (53, 54). In mice, Auten and colleagues found that the offspring of PM-exposed dams exhibited enhanced airway responsiveness, increased proinflammatory lung cytokine production, and increased mucous metaplasia when challenged with ozone compared with pups of mothers treated with filtered air (55). Zhu and colleagues found that mice deficient in the adipocytokine adiponectin were protected against ozone-induced inflammation and AHR (56). Similarly, Shore and colleagues reported that obese mice exhibited attenuated airway neutrophil recruitment in response to ozone as a result of impaired IL-6 release (57). Using knockout mice, Garantziotis and colleagues found that the matrix molecule hyaluronan played an important role in ozone-induced AHR (58). Matsubara and colleagues found that ozone-induced AHR was blocked by depletion of $V\gamma1^+$ $\gamma\delta$ T cells (59). Chuang and colleagues found that ozone exposure was associated with increased vascular oxidant stress and mitochondrial DNA damage (also observed in nonhuman primates) and dysfunction, and that ozone-exposed $ApoE^{-/-}$ mice exhibited accelerated atherosclerosis compared with air-exposed controls (60).

Bauer undertook a genetic analysis of *Inf2*, a quantitative trait locus associated with ozone susceptibility, in congenic strains of mice and identified MHC class II, the *Tnf* cluster, and other genes as potential contributors to the enhanced ozone susceptibility in this locus (61). Application of this method to larger regions of the genome is likely to identify other novel candidate genes that contribute to environmental susceptibility.

OCCUPATIONAL LUNG DISEASE

Occupational Asthma

The first reported longitudinal epidemiological study of "classic" acute irritant-induced asthma (also known as reactive airways dysfunction syndrome), although limited by its size, showed poor prognostic outcomes over an average of 13.6 years of follow-up, including little to no improvement in lung mechanics and poor psychological function, comparable to prior studies of allergic occupational asthma (62). This investigation suggests that outcomes of severe irritant-induced asthma are as poor as those of allergic occupational asthma.

Asbestos-related Lung Disease

An American College of Chest Physicians consensus statement described ongoing controversies in asbestos-related disease, based on a systematic assessment of expert opinion (63). Asbestos-induced ROS generation is critical for the development of asbestos-induced pulmonary toxicity and iron plays a role in their generation. Ghio and colleagues found minimal iron in asbestos-treated animals 1 day after instillation but significant staining 1 month later, suggesting an accumulation of iron over time (64). Several other molecular pathways have been implicated in the link between oxidative stress and inflammatory signaling after asbestos exposure, including increased EC-SOD–regulated syndecan-1 expression (65), protein kinase Cδ–dependent modulation of ERK1/2, C-Jun N-terminal kinase (JNK) 1/2, and Bim (66), DNA double-strand breaks in small airway epithelial cells (67), and Rac1 (68). Panduri and colleagues reported that mitochondrial 8-oxoguanine DNA glycosylase (Ogg1), which repairs 8-oxo-7,8-dihydroxyguanine (8-oxoG), one of the most abundant DNA adducts caused by oxidative stress, acts as a mitochondrial aconitase chaperone protein to prevent oxidant-mediated mitochondrial dysfunction and apoptosis (69).

Several large studies investigated the relationship between asbestos exposures (including chrysotile), asbestosis, and cancers of the pleura and lung (70, 71). Altomare and colleagues found that Arf inactivation promotes the development of mesothelioma through Fas-associated factor-1 (Faf1)–dependent tumor necrosis factor-α/nuclear factor-κB signaling (72). Ivanova and colleagues found that exposure of human malignant mesothelioma cells to asbestos caused transcriptional suppression of a novel tumor suppressor FUS1/TUSC2, which was down-regulated in human malignant mesothelioma tissue specimens (73). This effect was mediated via asbestos-induced ROS generation. Currie and colleagues showed that the programmed death ligand-1 (PD-L1; B7-H1) is highly expressed in malignant mesothelioma and that PD-L1 inhibitors activate antitumor $CD8^+$ T cells primarily in the absence of $CD4^+$ T cells (74).

Coal Workers' Emphysema

An autopsy study of U.S. coal workers, with careful quantification of structural lung changes and cumulative dust exposures in 722 miners and nonminers, demonstrated that not only is coal dust responsible for pneumoconiosis, it is associated with the development of emphysematous changes, even after accounting for smoking and at cumulative exposure concentrations below current U.S. regulations (75). Although prior work has demonstrated that coal mining is associated with obstructive lung disease, this study's detailed exposure and outcome assessments provide strong evidence to combat the general perception that the influence of smoking overwhelms that of coal dust on the development of obstructive lung disease. Given increasing global energy needs and increasing reliance on coal to meet those needs worldwide, the implications of this observation have substantial global occupational health importance.

Agricultural Workers' Pneumoconiosis

Although coal workers' pneumoconiosis is a well-recognized entity, a relationship between the inorganic dust exposures commonly encountered in agricultural work and pneumoconiosis has not previously been described. In an autopsy study of 112 Hispanic residents of Fresno County, California, Schenker and colleagues demonstrated changes consistent with pneumoconiosis and small airway disease, as well as crystalline silica and aluminum silicate particle deposits, in the lungs of farmworkers compared with nonfarmworkers (76). These observations suggest for the first time that farmwork may lead to pneumoconiosis, although the clinical implications are unclear.

Occupational Diesel Exposure and COPD

A 2009 retrospective cohort study of more than 30,000 U.S. railroad workers, with reliable data on years of diesel exposure and careful imputation of cigarette-smoking history, was the first cohort study to demonstrate that occupational diesel exhaust exposures are associated with COPD (77).

Novel Case Reports

Two novel potential causes of hypersensitivity pneumonitis (HP) were reported, including HP related to phytase, a bone-strengthening enzyme added to cattle feed (78), and HP with only indirect person-to-person contact to the putative antigen ("consort HP") (79).

A case series described parenchymal lung damage and restrictive lung disease associated with accidental inhalation of hydrochlorofluorocarbons (previously shown to have low pulmonary toxicity in animal studies) (80).

NANOPARTICLES

Many investigators have focused on the pulmonary toxicity of nanoparticles, particularly manufactured nanomaterials. Sydlik and colleagues studied the effect of compatible solute ectoine [(*S*)-2-methyl-1,4,5,6-tetrahydropyrimidine-4-carboxylic acid], which is known to reduce cell stress effects on carbon nanotube–induced lung inflammation in rats (81). Ectoine, when administered simultaneously or before the nanoparticles, reduced influx of neutrophils into the lung and MAPK activation and IL-8 release from lung epithelial cells in a dose-dependent manner. Folkmann and colleagues fed single-walled carbon nanotubes to rats and observed an elevation in the levels of the premutagenic 8-oxo-7,8-dihydro-2′-deoxyguanosine, which was used as a marker for oxidatively damaged DNA in liver and lung, but no effect in colonic mucosa (82). This effect was not due to a change in repair activity of oxidized base. Lu and colleagues evaluated whether short-term *in vitro* assays that assess oxidative stress potential and membrane-damaging potency of a panel of metal oxide nanoparticles can be used to predict their potency to induce inflammation and concluded that potency in generating free radicals *in vitro* did not predict the ability of nanoparticles to induce inflammation (83).

ENVIRONMENTAL CLIMATE CHANGE AND RESPIRATORY DISEASE

The climate talks in Copenhagen that marked the end of 2009 reflected increasing international concern about the myriad impacts of global climate change. In addition to the growing body of evidence described demonstrating health effects of the traffic-related air pollutants that are also greatly responsible for climate change, temperature itself has demonstrable respiratory health effects. Adding to prior evidence that increased temperature is associated with mortality, a 2009 study of 12 large European cities found that increased temperature itself is linked to respiratory hospitalizations (84).

CONCLUSIONS

Careful epidemiological studies published in 2009 have confirmed the detrimental cardiopulmonary effects of air pollution, especially particulate matter and ozone, on cardiovascular and respiratory health. These effects persist even at the lower mean levels of exposure that have been achieved in most regions of the United States and the rest of the developed world. Epidemiologists have taken advantage of more carefully phenotyped human populations with better defined exposures to determine which patient populations are most at risk for complications related to particulate matter exposure and to identify changes in those populations after pollution exposure that might point toward mechanisms. Simultaneously, molecular genetic models are being applied to air pollution exposure to identify the molecular mechanisms by which they contribute to disease and to identify genetic abnormalities that might predispose individuals to air pollution–related changes. Continued progress has been made in understanding the molecular and genetic pathophysiology of occupational diseases that have been with us for years. These lessons are being applied to the study of novel materials simultaneous with their development in an attempt to identify particles with risk before their widespread use. Climate change, continued urbanization, and increases in climate-changing pollutant concentrations worldwide all represent major concerns at the end of the first decade of the twenty-first century, a "perfect storm" for occupational and environmental respiratory disease. Avoiding the associated increase in the burden of cardiopulmonary morbidity and mortality, and its economic impacts, will require the concerted efforts of policymakers, guided by science, throughout the world.

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