The carcinogenicity of outdoor air pollution

In October, 2013, 24 experts from 11 countries met at the International Agency for Research on Cancer (IARC), Lyon, France, to assess the carcinogenicity of outdoor air pollution. This assessment was the last in a series that began with specific combustion products and sources of air pollution and concluded with the complex mixture that contains all of them. The results of this most recent assessment will be published as volume 109 of the IARC Monographs.[1]

Outdoor air pollution is a mixture of multiple pollutants originating from a myriad of natural and anthropogenic sources. Transport, power generation, industrial activity, biomass burning, and domestic heating and cooking are the predominant anthropogenic sources in many locations.[2] The mix of pollutants in outdoor air varies substantially over space and time, showing not only the diversity of sources, but the effect of atmospheric processes, including oxidation and weather. Diverse approaches are used to measure air pollution and some countries have established monitoring networks that typically record levels of regulated pollutants, such as respirable particulate matter (PM_{10}), fine particulate matter ($PM_{2·5}$), NO_2, SO_2, and O_3. $PM_{2·5}$ is increasingly used as an indicator pollutant, with annual average concentrations ranging from less than 10 to more than 100 μg/m³ globally. Pollution levels in western Europe and North America have generally declined since the late 20th century, but they are increasing in some rapidly industrialising countries, notably in Asia. In many areas, WHO and national air quality guidelines for $PM_{2·5}$ and other pollutants are routinely and substantially exceeded.[3] Occupational exposures to outdoor air pollution, although not routinely monitored, are also of concern for certain groups of workers, such as traffic police, drivers, and street vendors.

The IARC Working Group unanimously classified outdoor air pollution and particulate matter from outdoor air pollution as carcinogenic to humans (IARC Group 1), based on sufficient evidence of carcinogenicity in humans and experimental animals and strong mechanistic evidence.

The findings regarding the carcinogenicity of outdoor air pollution as a mixture, and of particulate matter specifically, are remarkably consistent in epidemiological research, studies of cancer in experimental animals, and a wide range of studies of mechanisms related to cancer. Particularly, an increased risk of lung cancer was consistently observed in cohort and case-control studies including millions of people and many thousands of lung cancer cases from Europe, North America, and Asia. The largest and most informative studies were a pooled analysis of data from ten European countries and a large nationwide cohort study in the USA.[4,5] Many studies estimated quantitative levels of outdoor air pollutants, most often as mass concentration of particulate matter, and adjusted for a wide range of potential confounders including tobacco smoking. Increased risk associated with outdoor air pollution was also seen in studies restricted to never smokers.[6] Positive exposure-response relations were consistently observed in studies that provided such data. Notably, virtually all of the studies were done in areas where annual average levels of $PM_{2·5}$ range from about 10 to 30 μg/m³, which represents approximately the lower third of exposures worldwide. Nevertheless, increased risk of lung cancer was observed even in those areas where $PM_{2·5}$ concentrations are less than the current health-based guidelines.[4]

There was limited epidemiological evidence for bladder cancer associated with various metrics of exposure to outdoor air pollution, including occupational and residential exposure to traffic or traffic emissions, in studies that were adjusted for tobacco smoking. However, most studies assessed exposure only by employment in occupations with potentially high exposure to outdoor air pollution, so the results did not weigh heavily in the evaluation.

The Working Group also reviewed evidence regarding the carcinogenicity of outdoor air pollution in experimental animals. As part of this process, the IARC's earlier evaluations of diesel engine exhaust and of emissions from the combustion of coal and wood were updated and confirmed. All of these agents can be present in outdoor air and were shown previously to cause benign and malignant lung tumours in mice or rats.

Only a few studies have assessed the occurrence of cancer in animals exposed directly to outdoor air pollution by inhalation. Studies of mice exposed to traffic-related outdoor air pollution in São Paulo, Brazil, showed an increase in the incidence of lung adenoma, and an increase in the incidence and tumour multiplicity of urethane-induced adenomas in a dose-dependent manner.[7] Several studies in which mice were injected subcutaneously with organic solvent-extracted material from particles collected from outdoor air pollution, showed increased incidence of injection-site tumours, including fibrosarcomas, and pulmonary adenoma or adenocarcinoma.[8,9]

The findings of carcinogenicity in humans and animals are strongly supported by a large, diverse body of evidence showing genetic and related effects in exposed humans and animals and a wide range of experimental systems. Studies of people exposed occupationally to outdoor air pollution have shown enhanced frequencies, relative to controls, of chromosome aberrations and micronuclei in lymphocytes.[10,11]

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Conflicts of interest

D H Phillips has received consultancy fees from Takeda and for litigation concerning asbestos-related disease compensation. G Hoek has received research funding from Concawe. A Russell has received research funding from Phillips 66, Southern Company, Electric Power Research Institute, and Health Effects Agency, and has consulted for EPRI and Health Effects Agency

Exposure to polluted outdoor air in occupational settings or urban and industrial areas is also associated with changes in the expression of genes involved in DNA damage and repair, inflammation, immune and oxidative stress response, as well as altered telomere length and epigenetic effects such as DNA methylation.[11] An increase of cytogenetic and DNA damage related to outdoor air pollution was associated with genetic polymorphisms, such as *GSTM1* null. Genetic damage, including somatic and germ-cell mutations, cytogenetic abnormalities, and DNA damage were also observed in mammals, birds, and plants exposed to outdoor air pollution.[12] Genotoxic effects have also been observed in studies of human and animal cell lines in vitro.

Additionally, extracts of particulate matter from outdoor air representing a wide range of locations, time periods, and atmospheric conditions induce mutations in bacteria. This mutagenic activity, covering more than five orders of magnitude per volume of air across locations, is quantitatively related to the concentration of atmospheric particulate matter. Thus, the Working Group concluded that there is strong evidence that real-world exposures to outdoor air pollution, in several species, are associated with increases in genetic damage, including cytogenetic abnormalities, mutations in both somatic and germ cells, and altered gene expression, which have been linked to increased cancer risk in humans.

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