

Carcinogenic Effects of Airborne Particles

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Ambient particulate matter (PM) comprises a heterogeneous mixture of substances including carbon, metals and organic matter, whose composition varies according to the predominant source of particles, season and prevailing weather. Recent epidemiological studies have demonstrated an association between PM and lung cancer, but the responsible mechanisms remain largely unknown, and crucial causal constituents are still to be identified.

In vitro and in vivo studies with coarse and fine PM sampled at various locations and seasons as well as model PM composed of ultrafine carbon black particles which has been coated with polycyclic aromatic hydrocarbons (PAH) and/or transition metals have revealed a likely role for multiple constituents and mechanisms in the genotoxic effects of particles. PM-associated transition metals, as well as particle-cell interactions lead to reactive oxygen species (ROS) formation and subsequent induction of oxidative DNA adducts and single strand breaks. Furthermore, PM samples can carry mutagens into the lungs, which can lead to formation of bulky DNA adducts. Apart from these genotoxic effects, PM as well as several of its constituents have also been shown to activate signalling pathways which are associated with inflammation, cell cycle regulation and proliferation, including Nuclear Factor-kappa B (NFkB) and Activator Protein-1 (AP-1). Importantly, ultrafine particles (<100nm) represent a major component of PM, which despite a negligible contribution to the over all particle mass, typically represent a extremely large surface area. This surface area and associated surface reactivity has been held responsible by toxicologists for a large number of acute and chronic biological effects of ultrafine particles in the respiratory tract including tumour formation.

Although exposure to airborne particles has been merely associated with respiratory tract cancer, extra-pulmonary malignancies can not be ruled out, as indicated from several observations. Firstly, biomarker studies in humans exposed to particles have demonstrated enhanced oxidative DNA damage (e.g. 8-OHdG), bulky adduct formation (e.g. PAH-DNA adducts) and mutagenicity (e.g. chromosome aberrations) in peripheral blood cells. Secondly, animal studies have demonstrated that inhaled particles, as well as certain compounds adsorbed onto their surface can elicit genotoxic and/or mutagenic effects in various organ systems including the blood, liver, bone marrow and germline cells. Finally, experimental studies with ultrafine model particles in human volunteers and animals indicate that the ultrafine component of ambient PM can translocate from the respiratory tract into various cancer-prone organs including the liver and the brain.

There is current consensus that children represent a crucial susceptible population in the respiratory effects of PM, e.g. since they spend more time exercising outdoors as well as being in their residential areas (home, nurseries, schools) when compared to adults. These aspects are associated with enhanced exposure to and inhalation of airborne particles. However, the possible role in which airborne particles play, with respect to childhood cancers, still remains to be elucidated.