Commentary

Genetic effects of air pollutants: insights from human biomonitoring studies

In this issue Sree Devi and coworkers report the results of a cytogenetic investigation on traffic policemen from an Indian metropolitan area. The study shows a distinct excess of cytogenetic damage in peripheral blood lymphocytes of policemen compared to indoor workers, highlighting the genotoxic consequences of the exposure to urban air pollutants. Genetic damage, for the severity and irreversibility of the effects at somatic and germ cell level, deserves the highest consideration, and may give an important contribution to the global burden of air pollution. Current estimates of the health impact of air pollution have largely been based on non-neoplastic outcomes, such as mortality for respiratory and cardiovascular diseases, even though outdoor air pollution is considered a significant risk factor for lung cancer in non-smokers. At present, the available evidence suggests that traffic-related pollution may be associated with childhood cancer and lung cancer in adults, with an estimated contribution of ~ 60,000 lung cancer deaths per year worldwide. Despite the increasing evidence for a role of air pollution in human lung cancer, especially in developing countries, there are still uncertainties on the underlying mechanism. Fine particles could initiate or promote the development of tumours with indirect mechanism(s), e.g., linked to the inflammatory activity of particulate matter, or through the direct genotoxic and promoting activity of their organic components. Extractable organic matter of ambient air in fact is known to be carcinogenic in rodents since decades, with hundreds of genotoxic components identified.

The chemical heterogeneity of air pollutants raises problems when human risk needs to be characterized. In this case relying on only one or a few chemically defined components can lead to considerable uncertainties in the estimate. Studies on exposure or early effect biomarkers can in principle provide an integrated measurement of the effect of complex chemical exposures. In this respect, biomarker studies in human populations exposed to air pollutants have allowed an improved exposure assessment, and contributed to shed light on potential mechanisms and individual susceptibility.

Among human studies, those using cytogenetic end-points as biomarker, have found most frequent application in investigations on the effects of air pollution. Cytogenetic biomarkers, notably structural chromosomal aberrations and micronuclei, have been shown to predict cancer risk at group level, and offer the premise to act as valid tools in cancer surveillance and prevention programmes in occupational and environmental health.

Several cytogenetic surveys have been performed in the past years on traffic policemen. These workers represent a convenient model population for evaluating the effects of outdoor pollutants, because they spend most of their workshift outdoor, usually in the most congested – and polluted – urban areas, thus experiencing a heavy exposure to vehicle exhausts. Even though traffic policing can be considered “worst cases” for the exposure to urban air pollutants, their profile of exposure is not dissimilar from that of other outdoor workers, e.g., newspapers vendors, and possibly of any other citizen spending most of his time outdoor. Thus biomonitoring studies on traffic policemen can provide information relevant for the whole urban population. Based on this premise, it is conceivable that studies undertaken in different geographical areas, with variable air pollution levels, provided variable results. Most studies performed in Western cities did not highlight significantly increased levels of cytogenetic damage in blood cells of traffic policemen compared to indoor workers. On the other hand, mainly positive results have been reported
from studies performed in developing countries, especially in Asia\textsuperscript{13-15}. This discrepancy most likely reflects the generally higher levels of urban air pollution which are nowadays typical of many densely inhabited areas in developing countries. Even though the quantitative relationship between cytogenetic damage in reporter cells and cancer risk has not been established, the two-fold increase in chromosomal aberrations in traffic policemen reported by Sree Devi and coworkers\textsuperscript{1} indicates a remarkable exposure to genotoxic compounds, which may underpin adverse effects at somatic and germ cell levels. In this respect it has to be taken into account that, despite the popularity of cytogenetic analysis on blood cells in human biomonitoring, this approach suffers a relatively limited sensitivity to \textit{ex vivo} chemical exposures. Chromosomal aberrations, as well as micronuclei and sister chromatid exchanges, are in fact only formed \textit{in vitro}, following mitogen stimulation of quiescent T lymphocytes: thus, the time elapsed between stimulation and fixation of primary DNA damage (normally the first DNA replication \textit{in vitro}) may allow the repair of most of damage induced \textit{in vivo} in circulating lymphocytes\textsuperscript{16}. Nevertheless in the study cited above\textsuperscript{1} the intensity of exposure to genotoxins from polluted air was able to induce chromosomal damage more efficiently than tobacco smoke. This does not mean that a parallel greater cancer risk is also expected, as both initiating and promoting agents co-operate in tobacco smoke carcinogenesis, but it helps to appreciate the severity of exposure, as in any case tobacco smoke represents a major source of exposure to genotoxins.

In common with other professionally exposed workers, traffic policemen experience a sustained exposure to noxious agents, which holds for most of their working time. This pattern of exposure may allow cumulative effects, if the induced damage is not adequately repaired. Circulating lymphocytes are to some extent an adequate target to reveal cumulative damage resulting from chronic exposure, as DNA repair capacity is reduced in quiescent lymphocytes because of the deficient intracellular deoxyribonucleosides pool\textsuperscript{17} and lower efficiency in nucleotide excision repair\textsuperscript{18}. Indeed data from the study of Sree Devi and coworkers\textsuperscript{1} confirm this view, showing an association between chromosomal damage and duration of exposure. This factor overlaps with age, which is by itself related with higher levels of chromosomal aberrations in both exposed and unexposed subjects. The latter result may reflect a decline in DNA repair capacity with age, as suggested by \textit{ex vivo} studies\textsuperscript{19}.

In conclusion, biomonitoring studies have repeatedly demonstrated increased levels of chromosomal damage in peripheral blood lymphocytes of traffic policemen compared to control subjects with no or limited exposure to air pollutants. Most of the evidence for an association between chromosomal damage and occupational exposure to air pollutants has been provided by studies performed in urban areas of developing countries, which are often characterized by high levels of air pollution. The excess of genetic damage observed in somatic cells (usually T lymphocytes) may imply an increased, albeit quantitatively undefined, cancer risk in other tissues. Importantly, these considerations apply not only to this category of professionally exposed workers, but to the whole urban population. The average intensity of exposure to air pollutants in traffic policemen is in fact not dissimilar from background levels of pollutants\textsuperscript{20}, to which are potentially exposed all subjects engaged in outdoor professional or recreational activities. Thus the evidence provided by biomonitoring studies on professionally exposed subjects should be considered as a warning for the whole urban population, which may comprise susceptible individuals at higher risk. In this respect, children should receive the greatest consideration. Children may differ from adults in rates of detoxification, DNA repair efficiency and cell proliferation rates, and thus be particularly susceptible from the long-term adverse effects of exposure to environmental genotoxins. Recent trends in childhood cancers\textsuperscript{21,22} seem to confirm this possibility, and indicate that the protection of children’s health must be a social priority, to be pursued also with the improvement of air quality in urban areas.

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\textbf{References}


