

Evoluzione della tossicologia industriale tra dosi effimere e genoma umano

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KEY WORDS

Biological monitoring; low doses; occupational exposure

SUMMARY

«Evolution of industrial toxicology: vanishing doses and genomics». Background: *This article aims to discuss the influence that the application of the recent discoveries in genomics will have on the theory and practice of industrial toxicology in developed post-industrial countries. It is stressed that the recent advances in toxicogenomics can be integrated into the existing wealth of knowledge on the toxic properties of industrial chemicals to improve the efficacy of prevention of toxicological risk.* Methods and Results: *The understanding of the biochemical and physiological mechanisms underlying susceptibility or resistance to the toxic effects of industrial xenobiotics, and in particular to carcinogens, allows us to split the epidemiologically derived relationship linking the frequency of disease in the exposed population to the level of workplace contamination into a set of sequential sub-relationships linking: a) the exposure level to that of workplace contamination; b) the internal dose to the exposure level; c) the biological effect (e.g., measured through biochemical markers of early effect) to the internal dose; d) the frequency of disease to that of observation of early biochemical effects. Each of the cited relationships is affected by a degree of uncertainty due to the variability of biological response among the examined individuals, which in turn requires a definition of the statistical limits for the association functions between the variables. As a consequence, the possibility of investigating the individual biochemical and physiological steps in the causal mechanism that links toxic exposure to disease does not necessarily lead to an increase in the information potential of biological monitoring, since the uncertainty due to inter-individual variability is amplified through the sequence of causal relationships to the point that the data from biological monitoring become valueless with regard to the prediction of the frequency or probability of disease. This is particularly true when exposure to 'low doses' is investigated, as is now increasingly frequent in post-industrial developed countries, where workplace contamination is now greatly reduced to levels which may be borderline with those in the general environment. Thus at the low-dose end of the range of contamination and exposure values there is an area where, for statistical reasons consequent to the heterogeneity of examined populations, a quantitative prediction of internal exposure due to environmental contamination, of biological adverse effects due to exposure levels and of frequency of disease due to the extent or frequency of biological effects is no longer reliably possible. This in turn impairs the preventive efficacy of biological monitoring.* Conclusions: *A closer integration between industrial toxicology and state-of-the-art molecular genetics derived from the recent sequencing of the human genoma is the way to overcome the limitations described. In particular, the individual subjects in the examined populations can be classified with regard to some genetically controlled characters relevant to the biotransformation of xenobiotics and to DNA repair and the statistical analysis of data can be performed on more homogeneous subpopulations, in order to decrease inter-individual variability of biochemical and physiological response. This in turn increases the predictive power of the biological markers, both of dose and effect, and improves the efficacy of prevention, e.g., by highlighting oversensitive subpopulations or lifestyles which can increase the risk of occupational and environmental disease.*