Oberdörster G. / University of Rochester

The respiratory tract as a portal for inhaled nano-sized particles

Although exposures to airborne nano-sized particles (particles <100 nm) have been experienced by humans throughout their evolutionary stages, it is only with the advent of the industrial revolution that such exposures have increased dramatically due to anthropogenic sources such as internal combustion engines, power plants, and many others. And, most recently, the rapidly developing field of nanotechnology is likely to become yet another source for human exposures to nano-sized particles – engineered NP – by different routes, *i.e*., inhalation, ingestion, dermal or even injection. Presently, we do not know the extent of expected exposure to engineered NP by any of these routes, whether inadvertent or controlled. Likewise, information on potential adverse effects is very limited at best. However, although potential adverse effects of engineered NP have not been systematically investigated, there are a number of studies that were performed in the area of inhalation toxicology and also human epidemiology from which some preliminary conclusions about effects of nano-sized particles can be drawn. These studies have tested the hypothesis that airborne ambient ultrafine particles (particles <100 nm) emitted from many anthropogenic sources (thermal degradation) contribute causally to increased morbidity and mortality in susceptible parts of the population. These effects have been observed in numerous epidemiological studies and have been attributed to particulate air pollution. In addition, there are some decades-old — mostly forgotten — studies with nano-sized particles which shed light on the biokinetics of such particles once introduced into the organism. Although there are differences between monodispersed engineered and polydispersed thermally-generated nano-sized particles, there are many similarities as well, and the same toxicological principles appear to apply. Collectively, therefore, from results of these older and new studies some emerging concepts of nanotoxicology can be identified which will be discussed. A major challenge lies ahead to answer key questions of nanotoxicology, foremost being the assessment of human and environmental exposure, the identification of potential hazards (toxicity *vs*. benefit), the biopersistence in cells and subcellular structures, the correlation between physicochemical and biological/toxicological properties and defining the appropriate dosemetric, the translocation pathways to sensitive structures within organs (biokinetics) as well as the mechanisms of uptake and translocation, and the mechanisms of effects at the organ/cellular/molecular level.

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