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General patterns and some peculiarities of organism's defensive and pathological responses to impacts of different metallic and metal oxides nanoparticles: A synopsis of results obtained in animal experiments

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In a series of experiments on rats we compared adverse health effects of spherical metallic particles in nanometer and, for some of them, also in micrometer range. We studied iron oxide (Fe_3O_4) nanoparticles produced by a chemical technique and nanoparticles of silver, gold, copper oxide, nickel oxide, manganese oxide, lead oxide and zinc oxide produced by laser ablation of respective pure metals in de-ionized water. In some experiments, we compared particles of one and the same composition having different diameters, while in others–equidimensional nanoparticles of different metals. For these comparisons we used 2 models: (a) a single intra-tracheal instillation in low doses 24 hrs before the broncho-alveolar lavage; (b) repeated intra-peritoneal injections during 6-7 weeks in non-lethal doses. All comparative assessments were based on experiments conducted strictly in parallel. Besides, we carried out a 10 months inhalation experiment with iron oxide (Fe_2O_3) aerosol produced by a sparking nanoparticles generator and fed to rats in the "nose only" system. It was found that the investigated nanoparticles were much more noxious on both cellular and systemic levels as compared with their fine micrometric or even submicron counterparts. However, within the conventional nanometer range the dependence of the organ-systemic toxicity on particle size is intricate and non-unique. Our data testify to a high activity of at least one of the key physiological defense mechanisms (pulmonary phagocytosis of deposited particles) against nanoparticles deposited in lower airways, while their noticeable solubilization in the biological milieus plays a more or less important role in toxicokinetics and toxicodynamics, depending on the nanoparticles size and chemical nature. There are, however, some important patterns of the *in vivo* toxic action common for all nanometals investigated by us–such as high cytotoxicity; as hepatotoxicity and splenotoxicity associated with nanoparticles' accumulation in RES-rich organs; as nephrotoxicity (mostly tubular) associated presumably with nanoparticles' active dissolution; and the last but not the least– heir "*in vivo*" genotoxicity. Taken together, these facts suggest that safe levels of exposure to metallic nanoparticles are possible in principle but should be very low.

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