Lead is a ubiquitous toxin and several biologic measures are available to assess its absorption, deposition, and health consequences. Blood lead (BLLs) and zinc protoporphyrin, commonly used measures, are poor predictors of health effects and are influenced by external exposure, internal lead stores, and interindividual differences in the toxicokinetics of lead. Other measures of lead absorption and burden have been developed (e.g., DMSA-chelatable lead, bone lead), but these have not been evaluated in prospective studies of health effects. Furthermore, there is little understanding of how individual factors may influence relations between these biologic measures and health effects. Increasingly, research has been directed at discovering interactions between individual factors and hazardous exposures. Interindividual differences in lead toxico-kinetics and toxicity are likely to be mediated, in part, by genetic factors, including polymorph-isms in proteins that differentially bind lead and affect its metabolism. Accumulating evidence suggests that δ-aminolevulinic acid dehydratase (ALAD), a polymorphic erythrocyte cytoplasmic enzyme, modifies lead's toxicokinetics. We propose a prospective study of the relations among BLLs, DMSA-chelatable lead, bone lead, and health effects (heme synthesis, renal early biologic effects and function, blood pressure, and CNS and PNS function) in lead workers in South Korea. Effect modification of these relations by ALAD genotype will also be investigated. This population is uniquely suited to investigation of gene-environment interaction because of its broad range of lead exposures, covering the entire range observed in the U.S., and large numbers of new hires. All current workers will be enrolled in the first year (N=640) and new hires will be enrolled for 2 years (N=230); these two groups will be compared with 120 nonexposed controls. Study measures will be obtained longitudinally, 3 times during the 4 year study. This proposal offers an understanding of the composite roles of BLLs, bone lead, and DMSA-chelatable lead, and effect modification by ALAD genotype, in the prediction of important health outcomes.

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