DEVELOPMENTAL EFFECTS OF METAL NEUROTOXICITY

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Increased exposures to trace elements can result in undesirable consequences for human health. Many trace elements are retained in the body for long periods and can be easily measured for the purpose of exposure assessment by inexpensive analytical methods. Thus, past and cumulated exposures can often be characterized from analysis of biological samples, such as blood and urine. Their validity depends on the time of exposure, time of sampling, and analytical quality.

Trace elements account for about half of the industrial chemicals that have so far been documented as developmental neurotoxicants – especially lead, methylmercury, and arsenic. These three trace elements were also among the first human developmental neurotoxicants to be discovered. They have contributed unique insights into developmental neurotoxicity and serve as paradigm neurotoxicants that provide a reference for other substances that may have similar adverse effects. Thus, while developmental neurotoxicity was originally thought to be a matter of specific toxicity from heavy metals, subsequent evidence now shows that the adverse effects are rather due to the extreme vulnerability of the developing brain.

Compelling evidence resulting from unfortunate past poisoning events has allowed scrutiny of long-term outcomes of acute exposures that occurred during early development. This evidence was followed by prospective studies of child cohorts. Due to the limited opportunities for repair and compensation, any damage that occurs to the brain of a fetus or child will likely remain for the rest of their life, though often modified due to functional plasticity and maturation.

These three neurotoxicants still pose a very real danger today. Even though lead toxicity is widely recognized by now, its adverse effects still occur as a result of reckless applications of lead in the past and our unwillingness to accept that a useful metal could be so harmful. In addition, methylmercury (MeHg) poisoning episodes in several countries clearly document that an exposed mother could escape unscathed, while her child might suffer serious mental retardation caused by the MeHg. There is therefore an urgent need to monitor the occurrence of elevated MeHg exposures in women who are or plan to be pregnant so that prenatal toxicity can be prevented. Furthermore, millions of children and pregnant women are regularly exposed to arsenic from contaminated drinking water. Serious arsenic contamination of the groundwater occurs in many countries of the world, where eroding minerals release arsenic to the water as a result of oxidation processes.

Other trace elements, such as manganese, cadmium, and fluoride, also appear to cause neurodevelopmental toxicity. Both manganese and fluoride are likely essential trace elements, and the findings of adverse effects on brain development therefore illustrate the fact that even essential trace elements may be toxic.

For lead, methylmercury, and arsenic, the evidence available today suggest that, with time, adverse effects were repeatedly documented at exposures previously thought to be “low” and safe. Recent discoveries on methylmercury indicate that mutations in at least a couple of genes can result in markedly different vulnerability to MeHg neurotoxicity. Exposure limits have been based on epidemiological associations

between exposures and adverse effects, but these associations represent the average vulnerability. Accordingly, the exposure limits are unlikely to protect subjects with a genetic predisposition.

Another concern is the imprecision of exposure assessments, often assumed to be excellent. However, toxicokinetics and biological variability add to the imprecision, and some measures may have a relative imprecisions (CV) of as much as 50%. As standard statistical analyses assumes no imprecision, the effects of the exposures are generally underestimated.

Developmental neurotoxicity results in lasting cognitive deficits and may also cause behavioral abnormalities. The societal implications are substantial. In this perspective, current prevention efforts in regard to trace elements known to be neurotoxic are insufficient.