HBM4EU science and policy for a healthy future

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HBM4EU

POLICY BRIEF

JULY 2022

European Human Biomonitoring Initiative

Lead

This policy brief summarizes the adverse human health effects of lead (Pb), its main exposure pathways for humans, and how human biomonitoring (HBM) of lead could be of value in the development of EU policies.

Lead is manufactured and/or imported in the European Economic Area in 1,000,000–10,000,000 tons per year. Secondary smelting (recycling) of lead from lead-acid batteries from vehicles and industries has become increasingly important and by the end of the 20th century accounted for almost half of world refined lead production. Other uses of lead include pigments, rust inhibitors, cable sheathing, plastic stabilizers and jewellery to name a few.

KEY MESSAGES

- Lead concentrations in blood showed a decreasing trend in the past decades due to regulations and recently levelled out at concentrations below the reference values set by different organizations.
- However, recent studies reported that lead exposure below the existing reference values is associated with adverse neurodevelopmental effects and suggested that there is likely no safe threshold for lead neurotoxicity. Foetuses and children are the most vulnerable and sensitive group to the adverse health effects of lead.
- Occupational exposure at certain workplaces (e.g. e-waste) and environmental exposures in some regions are still of concern.
- While there has been extensive research on lead as a substance, including its toxicology, recent human biomonitoring data is still relatively limited. This hinders interpreting population level exposure to lead across Europe and variations by geography and different key cohort populations.
- Monitoring exposure of the vulnerable populations and developing harmonised health-based guidance values and the validation of sensitive and reliable effect biomarkers is needed.

BACKGROUND: HBM4EU

The European Human Biomonitoring Initiative, HBM4EU, running from 2017 to June 2022, is a joint effort of 28 countries, the European Environment Agency and the European Commission, and co-funded under Horizon 2020. The main aim of the initiative is to coordinate and advance human biomonitoring in Europe. HBM4EU has provided a wealth of improved evidence of the actual exposure of citizens to chemicals and their possible health effects. Human biomonitoring allows us to measure our exposure to chemicals by measuring either the substances themselves, their metabolites or markers of subsequent health effects in body fluids or tissues. Information on human exposure can be linked to data on sources and epidemiological surveys to inform research, prevention, and policy with the objective of addressing knowledge gaps and promoting innovative approaches. If you would like to read more about the project itself, please visit the HBM4EU website.

HBM4EU RESULTS

To further support current and future HBM studies, HBM4EU has produced a variety of publicly available groundwork materials for a harmonised approach, to study planning and conduct in Europe, available in the HBM4EU online library.

The main outputs include the following:

- An overview of lead concentrations in the European population measured by human biomonitoring ranging from 1990 through to 2017 in 16 countries is summarised in the scoping document.
- A database including data on lead exposure (prior to HBM4EU) of more than 18,000 individuals from six European countries was compiled to investigate exposure determinants and trends.
- An overview of available health-based guidance values was provided in section 1.2 of the scoping document.
- Calculation of environmental burden of disease expressed as disability-adjusted life years (DALYs) based on HBM data of children and adults obtained from different EU countries, regions and hot spot areas was conducted as part of the project.
- In children, DALYs were estimated for developmental neurotoxicity (lost cognitive development attributable to Blood Lead Levels (BLL) above 20 µg/L. In adults, DALYs were estimated based on a recent dose–response relationship and corresponding hazard ratios (relative risk) between BLL above 10 µg/L and premature mortality (all causes of death).
- HBM4EU created an overview of the available human physiologically based pharmacokinetic (PBPK) models and conducted a review of the biomarkers of effect associated with lead exposure (Gundacker et al. 2021).
- A harmonized industrial hygiene and occupational human biomonitoring study was evaluated in eight European countries on the exposure of e-waste workers to lead, among others. One of the main findings was that e-waste workers are exposed to higher levels of lead compared to the control group.

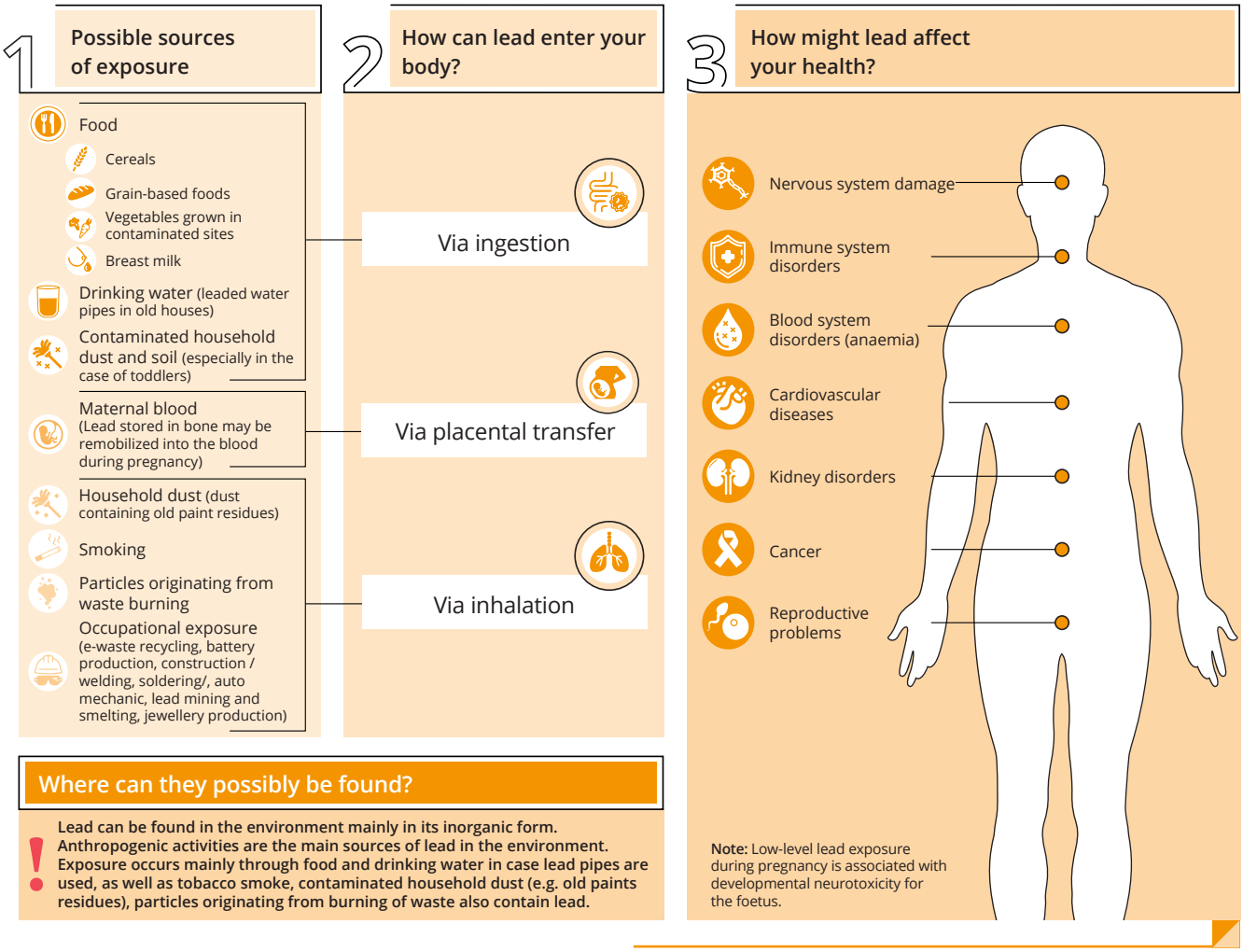
HBM4EU also laid the foundations for a European HBM Network to monitor human exposure to priority chemicals, including lead.

EXPOSURE & HEALTH EFFECTS

Whereas the exposure to lead in Europe is expected to be decreasing due to various regulations, the global consumption and exposure are increasing as the demand for storage batteries for electric vehicles rises (WHO 2010). Exposure levels vary geographically. People living in low-income regions with industrial uses of lead are more exposed. The most important source of exposure for the general population in Europe is the diet. In addition, the ingestion of contaminated soil and dust can be an important contributor for children.

An overview of main sources of exposure (environmental, occupational, consumer), exposure pathways (oral, inhalation, dermal) and health effects is provided in Figure 1.

Figure 1. Overview of exposure sources, pathways and health effects on lead



INPUT TO POLICY PROCESSES AND RELEVANT POLICY MEASURES

HBM4EU results have contributed to consultations for the Chemicals' Strategy for Sustainability, the Zero-Pollution Action Plan, as well as ECHA and EFSA consultations. These are available in the HBM4EU Science to Policy section.

Several policy measures have already been introduced in the EU to address human exposure to lead and manage risks. In general, the existing EU policies cover regulations on chemicals, the environment, consumer products and occupational exposure.

Lead is registered under REACH (Regulation (EC) No 1907/2006). Specific uses of lead are further restricted under Annex XVII (restriction), and lead has been identified as a substance of very high concern and included on the candidate list for authorisation. Lead is subject to EU harmonised classification and labelling under CLP (Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures).

The Drinking Water Directive (98/83/EC) limits the concentration of lead in water for human consumption to 10 µg/L. The Directive (EC) 2008/50 sets a regulatory limit value for lead in air as 0.5 µg/m3 per calendar year. The Directive (EEC) 86/278 sets a regulatory limit value of lead in soil as 50–300 mg/kg, in sludge for agriculture as 750–1200 mg/kg. Regulation (EC)1881/2006 set maximum levels for lead in foodstuffs (e.g., milk 0.020 mg/kg, crustaceans 0.50 mg/kg).

Occupational exposure is regulated by Directive (EC) 98/24 containing both a binding Occupational Exposure Limit (0.15 mg/m3) and a Biological Limit Value (70 µg/dL).

POLICY QUESTIONS

The answers to the policy questions below are summarised. For more details, please see the Substance Reports available on the substance specific page of the HBM4EU website.

1 What is the concentration of lead in human blood currently (after phasing out leaded petrol) in the countries of Europe?

Information on blood lead levels in children and young people after 2015 is limited, however the decreasing trend that followed the phasing out of leaded petrol came to a halt around 2010 in the countries with regular nationwide surveys and stabilized at approximately 10 µg/L. Although the blood lead concentrations were below the reference values set by different organizations, the most recent studies reported health outcomes even at lower concentrations, and it was suggested that there is likely no safe threshold for lead neurotoxicity.

2 Do blood lead levels of both adults and children still indicate permanent existence of lead exposure?

The data collected in HBM4EU showed the decreasing exposure of the European population over the past decades that levelled out in 2010 which indicates permanent existence of Pb exposure. However, data on the most recent exposure is lacking for Europe.

3 What are the sources of existing lead exposure in different European countries?

Based on the literature review, it is assumed that some foods, particularly cereals and grain-based products, may still contain lead at non-negligible levels when the raw materials had been grown at contaminated sites. Tap water from lead pipes in non-renovated old houses can also be a source of lead exposure. Old paint can also contain lead, as well as household dust. Furthermore, exposure to lead occurs through smoking and inhaling particles from burning waste and certain workplaces may present risk of occupational exposure. Furthermore, herbal and traditional medicine or cosmetics could be sources of exposure as well for some people. Lead can accumulate in certain parts of the body, thus the transplacental and breast-milk-mediated exposure of European women with relatively high age at childbirth is of concern. The high variation in breast milk Pb levels and the high concentrations found in some studies suggest that breast milk can pose a source of exposure for infants in some areas.

4 What kind of exposure sources are the most important for the children of various age groups and the younger or older adult population?

Based on the literature review, milk and cereals are the most important sources of lead for children, and grain-based foods for adults.

In some more deprived and polluted areas, children's Pb exposure can be of concern.

5 Taking the hazard from transplacental lead exposure of the unborn child into consideration, what are the blood lead levels of pregnant women?

Based on the literature review, the mean maternal and cord blood Pb concentrations did not exceed the EFSA BMDL01 value of 12 µg/L in the European surveys implemented after 2005. Lead concentrations were only slightly lower in cord than in maternal blood, indicating that the placenta does not constitute a barrier for Pb transfer from the maternal to the foetal compartment.

The toxicokinetics of lead has been studied extensively using experimental studies and modelling and different toxicokinetic models are available to predict blood lead concentrations. The extension of the physiologically-based pharmacokinetic model to pregnancy would be needed to fully assess the foetal exposure.

5 **Taking the presumably low concentration of lead in blood, is it feasible to measure blood lead levels in children from a small amount of blood as it can be from capillary samples? What criteria should be applied in order to avoid contamination from outside sources?**

Lead was not investigated within the HBM4EU Aligned Studies therefore, this question cannot be addressed.

5 **As it is difficult to connect later outcomes with exposures, which biomarkers of effects can be used in relation to effects caused by lead exposure?**

There is not sufficient information for mandatory inclusion of specific effect markers in future HBM studies concerning lead exposure associated with neurodevelopmental disorders. Reduced brain-derived neurotrophic factor (BDNF) is a potential biomarker of Pb-induced neurotoxicity that should be further investigated. BDNF is a key regulator of brain development and neural plasticity and is involved in the pathophysiology of diverse neurological and psychiatric disorders. BDNF can be assessed in different biological matrices and at different exposure levels. Among other environmental chemicals, including bisphenols, phthalates and polycyclic aromatic hydrocarbons can influence the expression and regulation of this protein.

Epigenetic changes due to environmental exposure, including DNA methylation, can influence BDNF expression and regulation, thus the DNA methylation status of the BDNF gene seems to be another (more stable) biomarker of neurotoxic effects caused by lead exposure.

KNOWLEDGE GAPS

HBM4EU has helped to identify a number of specific data gaps that are needed to give policy makers relevant and strategic data to establish appropriate regulations and improve chemical risk management. However, some gaps and needs for action remain:

- Long-term monitoring of exposure levels to evaluate differences between countries and population groups, time trends, and age-related differences in exposure.
- Establishment of an age specific health-based human biomonitoring guidance value, especially for the vulnerable target groups.
- Establishment of standardised non-invasive methods for assessing lead exposure, especially in the case of children.
- Validation of sensitive and reliable effect biomarkers to assess the exposure.

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