Human Biomonitoring - ethical and practical considerations

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Environmental medicine

- Studying interactions between environment and human health
- Performing health risk assessments
  - hazard identification
  - dose-response determination
  - exposure assessment
  - risk characterisation

The environmental public health continuum
Humans and the environment

- Air/dust
- Food
- Skin contact
- Water
Techniques in exposure assessment

• Measuring concentrations in delivering media, e.g. food, and calculate intake from intake factors

  → External dose

• Biomonitoring, i.e., measure chemicals or reaction products in human biological matrices

  → Internal dose

"Pollution gets personal"
Concentrations of brominated flame retardants in foods

Table 1: Concentrations of PBDEs and HBCD in foods used in exposure calculations. Data are shown as ng/g fresh weight. LB = lower bound, UB = upper bound concentrations, n = number of analyses.

<table>
<thead>
<tr>
<th>Food</th>
<th>PBDE-28</th>
<th>PBDE-47</th>
<th>PBDE-99</th>
<th>PBDE-100</th>
<th>PBDE-153</th>
<th>PBDE-114</th>
<th>PBDE-83</th>
<th>PBDE-289</th>
<th>HBCD</th>
<th>HBCD</th>
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<tbody>
<tr>
<td>Farmed trout</td>
<td>0.298</td>
<td>0.389</td>
<td>0.460</td>
<td>0.434</td>
<td>0.049</td>
<td>0.080</td>
<td>0.010</td>
<td>0.010</td>
<td>0.334</td>
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<tr>
<td>Wild trout</td>
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<td>0.389</td>
<td>0.460</td>
<td>0.434</td>
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<tr>
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<td>0.330</td>
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<tr>
<td>Biscuit</td>
<td>0.330</td>
<td>0.330</td>
<td>0.330</td>
<td>0.330</td>
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<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.97</td>
<td>0.97</td>
</tr>
</tbody>
</table>

*HBCD sterioisomomers have not been determined separately, sum HBCD has been set as o-HBCD.*
Dietary exposure to brominated flame retardants

Concentrations in foods; ng/g

Food consumption from food frequency questionnaires and gender specific portion sizes; g/day

Table 2: Dietary PBDE (ng/kg body weight/day) exposure based on mean lower bound concentrations in food.

<table>
<thead>
<tr>
<th></th>
<th>All participants, including reference group, n = 184</th>
<th>Reference group, n = 73</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean  Median  95-perc  Min  Max</td>
<td>Mean  Median  95-perc  Min  Max</td>
</tr>
<tr>
<td>Sum 5 PBDE&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.40   1.06   3.66   0.14   7.00</td>
<td>1.03   0.74   2.78   0.14   3.45</td>
</tr>
<tr>
<td>Sum 7 PBDE&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.47   1.11   3.84   0.14   7.36</td>
<td>1.08   0.77   2.94   0.14   3.63</td>
</tr>
<tr>
<td>HBCD&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.33   0.27   0.83   0.06   1.35</td>
<td>0.27   0.23   0.60   0.06   0.87</td>
</tr>
</tbody>
</table>

<sup>a</sup>Sum BDE-47, BDE-99, BDE 100, BDE 153, BDE 154.  
<sup>b</sup>Sum 5 PBDEs + BDE-28 and BDE-183.  
<sup>c</sup>Sum α-HBCD, β-HBCD, γ-HBCD.
Toxicokinetics of environmental chemicals
Types of human samples used in HBM

• Invasive: organ and adipose tissues, teeth, blood
• Non-invasive: breast milk, urine, saliva, semen, hair, nails, exhaled breath, meconium
Advantages of HBM

- Integrated exposure from various routes, sources, environments
- Demographic factors, lifestyle factors
- Identification of vulnerable populations and groups at higher risk
- Identification of public health threats before diseases become evident, policy action
Limitations and Obstacles for HBM

- Often invasive sampling necessary
- Cost-intensive for large cohorts
- Lack of harmonized approaches
- Limited knowledge on toxicology and health impacts
- Approval by Committees for Medical and Health Research Ethics
- Biobank Act, Personal Data Act
Use of HBM data

- Establish baseline levels of chemicals in populations, temporal and geographical trends
- Identify higher exposed populations at risk
- Evaluate relationships between internal dose and health outcomes
- Take action to protect public’s health
- Assess the effectiveness of bans and regulations
Use of HBM in environmental health

• **RESEARCH projects**
  – knowledge on causal links between environmental factors and health
  – *hypothesis generation and testing*

• **SURVEY projects**:  
  – prevalence of exposure to environmental agents and the related public health impact
  – *develop and evaluate policies that protect health*

• **CAMPAIGNS (Action Group activities)**
  – demonstrate exposure to pollutants
  – to raise awareness & need for policy
Research project

Hypothesis: Increased obesity in postpubertal female mice upon prenatal exposure to PFOA is also valid for humans.

Method: A prospective cohort of 665 Danish pregnant women recruited in 1988-1989 with offspring follow-up at 20 years. PFOA was measured in serum from gestational week 30.

Results: Comparing highest to lowest quartile (median: 5.8 vs. 2.3 ng/mL) in maternal PFOA concentration resulted in adjusted relative risk of 3.0 of being overweight or obese (BMI, waist circumference) among female offspring.

Conclusion: Low dose developmental exposures to PFOA are in line with experimental results suggesting obesogenic effects in female offspring at postpubertal age

Halldorsson et al., EHP in press
Surveillance projects

- Monitoring time trends of chemical concentrations in the population
- Validation of the effectiveness of regulation
- Targeted assessment of populations suspected to be at environmental "hotspots"
- Investigating "clusters" of disease that might be related to an environmental exposure
- Detecting emerging exposures that were unsuspected
Trends in PBDE levels in humans from Norway and Sweden

D.M. Guvenius, PhD Thesis, 2002; Thomsen et al. 2002
Campaigns: Raising awareness of the extent of chemical pollution in Europe

WWF has organised 8 biomonitoring surveys in the past 3 years, testing around 350 people across Europe

• Chemical check-ups to test for the presence of potentially harmful chemicals in human blood (2003)

• 40 members of the European Parliament, 14 Ministers throughout Europe, doctors and scientists, celebrities

• 3 Generations of 13 European families (spring 2005).

People are contaminated with a cocktail of persistent, bio-accumulative and toxic man-made chemicals.
Ethical aspects of HBM

The collection of human samples and data is subject to regulations and rules to protect the individual’s rights and interests and guarantee respect for human dignity and the equality of moral status of all individuals.
Framework of Biomedical Research Ethics

- International conventions and declarations
  - Helsinki Declaration: Ethical principles for medical research involving human subjects (WMA 1964)
  - Oviedo Convention of the Council of Europe (1979)
  - UN Convention of the Rights of the Child (1990)
- Guidelines and Recommendations for Ethical Committees
- Opinions
  - European Group on Ethics, Council of Europe
Conventional bioethical principles

• Autonomy: respect for humans
• Beneficence: do good for people
• Nonmaleficence: do no harm
• Justice: balance between benefits and costs
• Veracity: tell the truth, present information in an objective way
• Confidentiality: right to privacy
How do these principles work?

- Not rigid rules or prohibitions, but offer guidance
- Practical compromises required
- Form the basis for the work of Research Ethics Committees
Ethics Committees

Any research project involving humans requires ethical approval from research ethics committees before initiation.

US: Institutional Review Boards (IRB)
Europe: Regional (Institutional) Research Ethics Committee

The purpose of the review is to assure that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in a research study.
Regional Ethics Committees

- Application form
- Study protocol
  - study aim and hypotheses (scientifically valid)
  - selection, recruitment of study persons
  - sampling, biobanking, processing, analysis
  - results and interpretation, data storage (privacy)
  - information strategy prior, during and after study
- Invitation letter, informed consent
- Questionnaires
An explanation of the purpose of the research and the expected duration of the subject's participation

A description of the procedures to be followed and identification of any procedures that are experimental

A description of any foreseeable risks or discomforts to the subject and a description of what steps will be taken to prevent or minimize them

A description of any benefits to the subject or to others that may reasonably be expected from the research. Monetary compensation is not a benefit. If compensation is to be provided to research subjects or healthy volunteers, the amount should be stated
Informed consent document

- A statement describing to what extent records will be kept confidential, including a description of who may have access to research records
- An explanation of whom to contact for answers to pertinent questions about the research and the research subject's rights
- A statement that participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled.
Check list for informed consent

• Is it written at a reading level understandable to research subjects?
• Is the document formatted well? Does it have headings which break the text into short sections?
• Does the document contain the basic elements for informed consent and are they presented in a clear, easy-to-understand way?
• Can the document be shortened without compromising clarity or other requirements?
Confidentiality

• Assure that identifying information is not made available to anyone who is not directly involved in the study
  – **Identifiable**: name or personal number on sample (not possible)
  – **Coded data**: Coded data: sample has no personal identification, only a code (store link between code and names in safe accessible only to project leader)
  – **Anonymous**: no link from sample to person (no privacy problems)
Communication of results

A. At individual level
   – the lack of relevance of the results at individual level
   – too limited time and/or resources; and
   – fear of causing (unnecessary) alarm
   – scientific uncertainty
   – lack of potential for remediation.

B. At collective level
   – participants in general terms as a group
   – the general public
   – other authorities on the potential health consequences or on measures for policy development and prevention
Communication of results

• Dilemma “Duty to inform” vs. uncertainty in data interpretation
  – Healthy volunteers, may create anxious reactions
  – Pure results are of no individual use, need to put into perspective and interpreted. On request only.
  – NHANES: Test results are not given unless the concentration is markedly above population means (source identification and reduction)

• Communication strategy must be included in the research protocol from the beginning!
Trout from Lake Mjøsa is highly contaminated with PBDE
Hobby anglers from Mjøsa have higher blood levels of PBDE than controls
PBDE blood levels are correlated with intake of trout
Consumption advisory for trout from Mjøsa

Based on the occurrence of Hg and dioxins/dl-PCBs

- Children and women in fertile age shall not consume trout more than 4 x p.a
- Pregnant or nursing women shall not consume trout > 1kg
- People shall not consume trout > 1kg more than once per month on average
Risk assessment

• 11 of 64 participants had a calculated intake of dioxins /dl-PCBs > 14 pg TEQ/kg bw/week (EUs TWI) corresponding to what is found in the general Norwegian population.

• No women in fertile age among those exceeding TWI.

• TWI developed with safety margins considering differences in susceptibility between animals and humans and between humans.

• Present knowledge of the toxicology of PBDEs indicate that the exposure is covered by existing consumption advisories.
Balancing risk and benefits

- Hobby anglers consuming lake Mjøsa trout are at risk for high intake of POPs and Hg
- Hobby anglers gain health benefits from their recreational fishing activities