Human Biomonitoring

Introduction

EU Policy

AT Pilot Project

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outline

- Definition
- examples
- European context
- Requirements

- Humanbiomonitoring in Austria
- Conclusion

- Evaluation, Interpretation, Measures

Human Biomonitoring

- Monitoring of **Biomarkers**
  - Determination of human exposure to chemicals
  - Determination in e.g. blood, teeth, scalp hair, urine, breast milk,…
- Uptake of chemicals
  - Measurement of the parent compounds or metabolites
    - Dosis monitoring
  - Reaction of organism provoked by chemicals
    - Effect monitoring

Ambient monitoring	
Biomonitoring/Dosis	
Internal dosis = dosis monitoring	Effective dosis = biochemical effect monitoring
Substances and metabolites in liquids, tissue	Protein, DNA adducts liquids, tissue
Biomonitoring/Biomarkers of effect	
Change of enzyme activity Changed cytogenetic parameters (genotoxicity)	
Change of genetic structure or function Mutation Activation or deactivation Change of organ functions	
Health Effects	

Dosis monitoring

- Determination of the overall exposure
  - Unerring and independent of exposure routes
    - Sources as food, air, water, soil,…
    - Routes as inhalative, oral, dermal,…
  - Influence factors
    - Chemical/metabolism
    - detoxification
    - genotypes
    - physiology
    - Lifestyle and habits
  - Target Human Being
  - Restriction
    - Exposure depends on metabolism
    - Images only a limited time back
- Chemcials?
  - Highly specific for individual chemical
  - But not for certain effect (and vice versa)

chemicals

- Urine
  - Metals
  - organic solvents
  - PAHs
  - Phthalates
  - Phytoestrogens
  - Industrial chemicals
  - Pesticides
  - Phenols
  - cotinine
- blood
  - PCBs
  - Dioxins
  - PBDE
  - Trisphosphates
  - PFCs
  - Polycyclic musk cpd.
  - Heavy metals

Human Biomonitoring

- HBM is an **instrument** to
  - determine the **exposure** independent of exposure routes
  - detect abnormalties
    - **regional**
    - **individuell**
    - **collective**
    - national/european **reference values**
  - **policy** (EU/AT)
  - potential threats (**early warning system**)
  - evaluation of **effectiveness** of measures (i.g. REACH, non-smoker protection,…)
- **Integrated assessment** along with
  - environmental data/ envrionmental monitoring
  - toxicological data
  - ecotoxicological data
  - effects

comparability of data-harmonisation

history

- originally: element of occupational medicine
- 20 years of tradition in environmental medicine
  - NHANES (USA: CDC)
  - DE. Kinder-Umweltsurvey (DE)
- 77/312/EEC on biological screening of the population on lead
  - First image of lead burden in citizens
- Environment and Health Action Plan 2004-2010
  - Action 3 – EU wide harmonized human biomonitoring
- WHO ministerial conference Parma 2010
  - Reference to human biomonitoring

requirements

- What is needed for setting up a HBM programme?
- Extent of programme
  - Local knowledge of dosis
  - General overview
  - Reference values

requirements

- Study groups – donating samples
  - Representativity (for whom, what?)
    - General population
    - Occupational exposed people
    - Hot spots
  - Socio-economical factors
    - Income
    - Housing
    - Habits
    - Lifestyle
- Questionnaire
  - Guided or self comleted?

requirements

- Sampling
  - Ethics approval
    - Invasive/non invasive – children
    - Preparation of dossier
    - Privacy statement
    - Commitment of study persons
  - Sampling
    - Clinics
    - Home
    - Attendance
  - Storage/conservation
    - Centrifuge
    - Chemical conservation
    - Freezing

requirements

- Robust and comparable analysis
  - Laboratories available???
  - Standardized method (accreditation?)
  - Round robin tests
  - Expected range of levels
  - LOD/LOQ
  - Robust preparation
    - Legal requirements – security laboratory
  - Further data needed for interpretation
    - Blood fat or creatinine
  - Report format
  - Is privacy guaranteed?

requirements

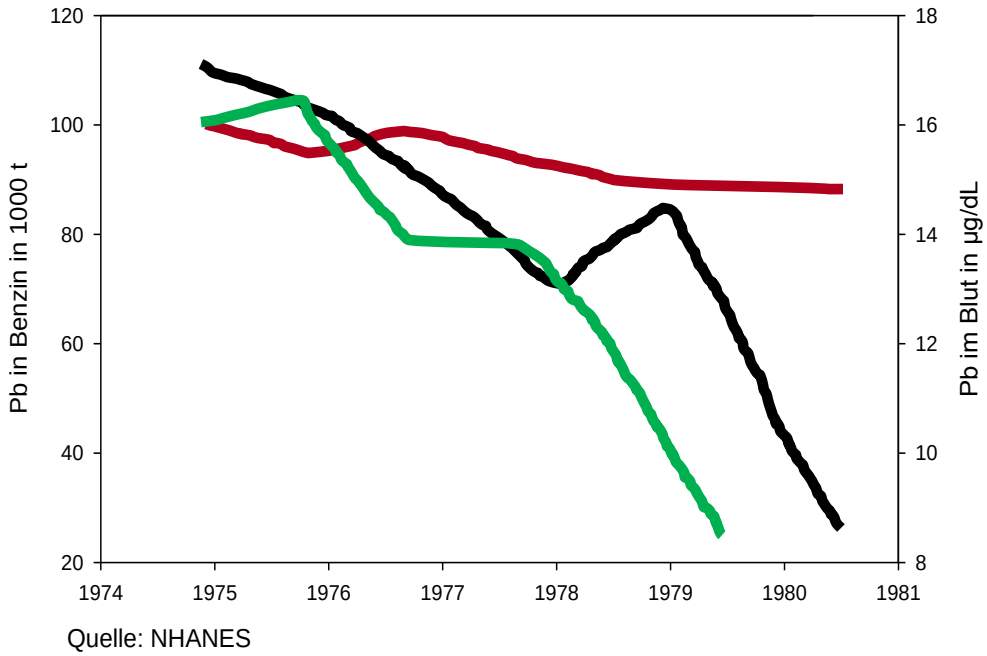
- General information about substances
  - Specific questions
- How to distinguish
  - High levels
  - Low levels
- Background levels
  - 90/95 percentile
- HBM levels (Germany)
  - Epidemiologically/toxicologically derived values

Relevance ?

	Occupational exposure	Environmental exposure
Exposure regarded as	High	low
time	35 years 220 d/a 8 h/d = 62.000 h	80 years (avg. m+w) 365 d/a 24 h/d = 700.000 h
Risk	?	?

- **Relevance of environmental exposure in terms of time of exposure**

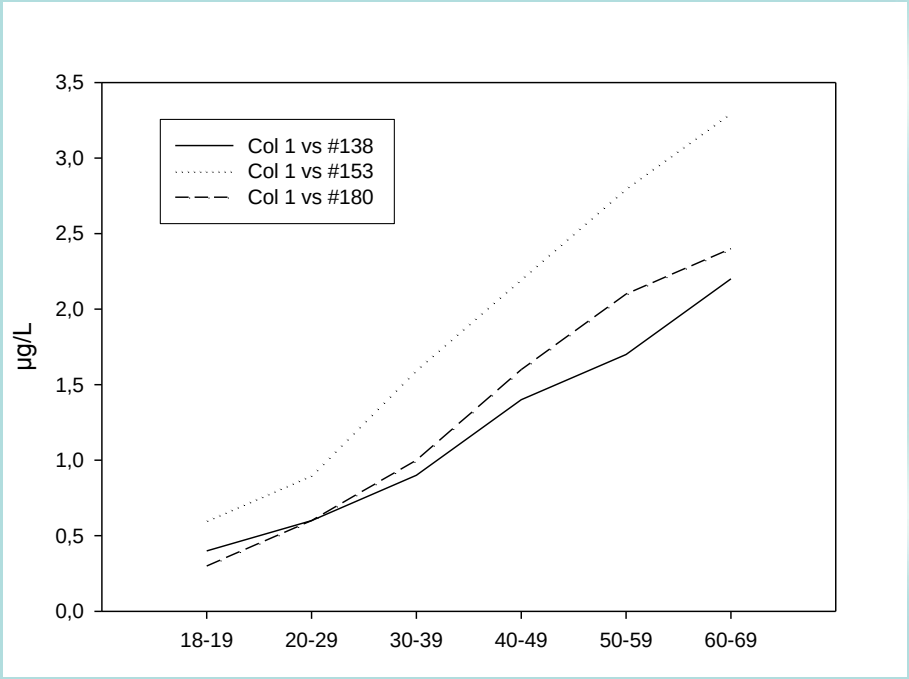
Example lead



Quelle: NHANES

- Reduction of Pb in petrol in US
  - black line
- Prediction of Pb in blood
  - red line
- Effective reduction was directly linked to reduction of the source
- Models not always reliable
  - Pb vs. POPs

Example PCB



Quelle: KUS

- Bio accumulating – the older the higher he blood level
- Differenciation necessary
- Therapy by reduction of sources

Further examples

- Pentachlorophenol (PCP) indoors
  - Sick building syndrome
  - No abnormalities in dust analysis
  - High level of PCP
  - Indirect source identification by means of HBM

- Expertise Umweltbundesamt
  - Nonylphenol, Bisphenol A – Harn (AKH)
  - Polycyclic musk compounds – blood (MedUni)
    - Two studies
  - Framework of a indoor air study (MedUni)
    - Hair and milk teeth of school children – heavy metals

internationally

- Request for harmonised approaches in Europe
- Request for comparability of data
  - Recruitment strategy
  - Sampling
  - Analysis
  - Evaluation
- European Enviromental Health Action Plan 2004-2010
  - Action 3
- WHO
  - Ministerial declaration 2010 (Parma)

Commitment of the European Commission

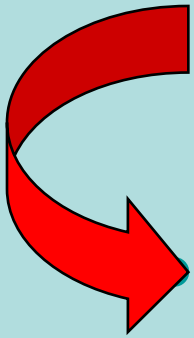
health is a central issue in environmental policy

Support of environment-and-health policy

By means of better comparability of data, access to data resource efficiency through common development of scientific instruments and strategies

Aktivitäten

- ESBIO
  - **E**xpert Team to **S**upport **Bio**monitoring in Europe
  - Elaboration of basic protocols for the implementation of a HBM network in Europe
  - goal
    - "pilot project" Human Biomonitoring in Europe
    - Harmonised "learning by doing"



- COPHES
  - **CO**nsortium to **P**erform **H**uman biomonitoring on a **E**uropean **S**cale
  - FP7 Network of Excellence
  - 24 MS
  - National co-financing through Lebensministerium

Activities

- High number of proposals vs. limited financial means
  - COPHES was rejected
  - Official letter in summer 2008
- COPHES II
  - Coordination action (FP7)
  - COPHES II accepted for funding (inoff.)
- DEMOCOPHES
  - LIFE+
  - DEMOCOPHES rejected, but second submission in autumn 2009

Activities

- „Humanbiomonitoring study in Austria“
  - Started 2008
  - Funded by Lebensministerium
    - Former COPHES national contribution
  - Partner Medical University of Vienna
  - Sampling/Measurement 2009
  - Evaluation/Reporting in 2010
  - Still compatible with EU projects

Humanbiomonitoring AT

- Representative cross-sectional study
- Radom selection of regions
  - > 1 Mio. inhabitants
  - 1 Mio. - 100.00 inhab.
  - 100.000 - 10.000 inhab.
  - 5.000 – 10.000 inhab.
  - < 5.000 inhab.
- Random contact by telefone
  - Exclusion list
- Guided interview questionnaire
- Sampling and questionnaire at home of test persons

Humanbiomonitoring AT

Biomarker	Matrix	Test group	Nr.
Trisphosphates	Blood	Adults	100
PBDE	Blood	Adults	100
Phthalates	Urine	Mother & child	100
NP, OP, BPA	Urine	Mother & child	20

Mothers and adults: 22-50 years
children: 6-11 years

Substances

- Trisphosphates
  - Use as flame retardant and softener
  - High production chemical/turn over
  - Chlorinated Trisphosphates: neurotoxic
  - Acute and chronic intolerance

- Phthalates
  - Softener in plastics
  - High production and turn-over numbers
  - Endocrine effects

substances

- Polybrominated Diphenyl ethers
  - Similar to PCB (Polychlorinated biphenyls)
  - Flame retardants
  - High production and turn-over
  - persistant, bio-accumulating, liposoluble (recently Stockholm convention)
  - affects nervous a. brain development, cognitive defects, estrogenic effects
- Nonylphenol, Octylphenol, Bisphenol A
  - Monomer to plastics
  - High production and turn-over
  - Endocrine effective

Optional programme

- Proposed additional compounds
  - Samples already available

Proposal	Matrix	Test group	Nr.
Perfluorinated surfactants ("PFOS")	Blood	Adults	100
Me-Hg	Hair	Mother and child	100
Cotinine	Urine	Mother and child	100
Pb, Cd, Hg	Urine	Mother and child	100

Optional programme

- Perfluorinated surfactants
  - Recently included in Stockholm-convention
  - Special surfactant (indoor application)
  - High consumption, persistent, bio accumulative, toxic, not biodegradable
- Methyl mercury
  - Biotransformed – toxic form
  - Fish relevant source of uptake
  - Target organ: nervous system

Optional programme

- Cotinine
  - And further nicotin metabolites
  - >50% (!) of children are passive smokers
  - Determination in urine
- Pb, Cd, Hg
  - Determination in urine
  - Heavy metals (e.g. lead pipes)
  - smoking/environmental smoking
  - Inorganic Hg species (Hg)

summary

- Human biomonitoring is an important environmental and health diagnosis instrument
  - Diagnosis: effective exposure of the individual apart from exposure routes
  - Therapy I: deduction of recommendations for action (chemical policy, non-smoker protection, precautionary principle)
  - Therapy II: Evaluation of effectiveness of measures
  - Therapy III: trend studies
- Warning system
  - Unique identification of sources
- „stand alone" instrument
  - Integrative assessment with environmental/tox/effect data

evaluation

- Background levels (reference values)
  - Average burden of population
    - 90/95th percentile
- HBM values (Germany)
  - Tox./epidem. Based
  - Expert judgement by commission
  - HBM I
    - risk cannot be excluded
    - Check of values, 2nd measurement, search for sources
  - HBM II
    - Risk is possible
    - Medical assistance, urgent need for measures

Tabelle 2: Referenzwerte für polychlorierte Biphenyle in Vollblut und Blutplasma [8,9] und für Organochlorverbindungen im Vollblut [10]

Alter (Jahre)	**PCB-138** µg/l		**PCB 153** µg/l		**PCB 180** µg/l		**∑ PCB-138,-153,-180** µg/l		**β-HCH** µg/l	**HCB** µg/l
	Vollblut	Plasma	Vollblut	Plasma	Vollblut	Plasma	Vollblut	Plasma	Vollblut	Vollblut
7 – 10	0,5	--	0,5	--	0,3	--	1,3	--	0,3	0,4
18 – 25	0,8	0,8	1,0	1,0	0,7	0,8	2,5	3,2	0,2	0,4
26 – 35	1,0	1,5	1,5	1,9	1,0	1,5	3,5	5,6	0,4	1,2
36 – 45	1,3	2,2	2,0	2,8	1,4	2,2	4,6	7,6	0,7	2,1
46 – 55	1,6	3,0	2,5	3,7	1,9	2,9	5,7	10,0	1,3	2,9
56 – 65	1,8	3,7	3,0	4,6	2,2	3,5	6,8	12,2	1,3	4,0
> 65	Oberhalb des Alters von 65 Jahren liegen nur sehr wenige Daten vor. Es wird daher empfohlen, vorläufig die Referenzwerte der Altersgruppe 56 bis 65 Jahre heranzuziehen.								2,0	4,6

Referenzwerte			Human-Biomonitoring-(HBM)-Werte		
Analyt und Probenmaterial	Personengruppe	Referenz-Wert	Personengruppe	HBM-Werte HBM-I	HBM-II
Blei (Pb) im **Vollblut** [4]	Kinder (6-12 Jahre) Frauen (25-69 Jahre) Männer (25-69 Jahre)	60 µg/l 90 µg/l 120 µg/l	Kinder ≤ 12 Jahre und Frauen im gebärfähigen Alter Frauen > 45 Jahre und Männer	100 µg/l 150 µg/l	150 µg/l 250 µg/l
Cadmium (Cd) im **Vollblut** [6]	Kinder (6-12 Jahre) nichtrauchende Erwachsene (25-69 Jahre)	0,5 µg/l 1,0 µg/l		entfällt, da nach dem derzeitigen Erkenntnisstand HBM-Werte für Cd im Blut nicht sinnvoll ableitbar sind	
Cadmium (Cd) im **Urin** [6]	Kinder (6-12 Jahre) nichtrauchende Erwachsene (25-69 Jahre)	0,5 µg/g Crea. bzw. 0,5 µg/l 1,0 µg/g Crea. bzw. 1,5 µg/l	Kinder und Erwachsene ≤ 25 Jahre Erwachsene > 25 Jahre	1 µg/g Crea. 2 µg/g Crea.	3 µg/g Crea 5 µg/g Crea.
Quecksilber (Hg) im **Vollblut** [7,11]	Kinder (6-12 Jahre) bei einem Fischkonsum bis zu dreimal im Monat Erwachsene (25-69 Jahre) bei einem Fischkonsum bis zu dreimal im Monat	1,5 µg/l 2,0 µg/l	Kinder und Erwachsene	5 µg/l	15 µg/l
Quecksilber (Hg) im **Urin** [7,11]	Kinder (6-12 Jahre) und Erwachsene (25-69 Jahre) ohne Amalgamfüllungen	1,0 µg/ Crea. bzw. 1,4 µg/l	Kinder und Erwachsene	5 µg/g Crea. bzw. 7 µg/l	20 µg/g Crea bzw. 25 µg/l
Pentachlorphenol (PCP) im **Serum** [5,13]	Allgemein-bevölkerung	12 µg/l	Allgemein-bevölkerung	40 µg/l	70 µg/l
Pentachlorphenol (PCP) im **Urin** [5,13]	Allgemein-bevölkerung	6 µg/g Crea bzw. 8 µg/l	Allgemein-bevölkerung	20 µg/g Crea. bzw. 25 µg/l	30 µg/g Crea. bzw. 40 µg/l

- Reference, HBM I +II
  - Increasing need for action
  - Medical assistance
  - Search for source
    - Ethical requirement
  - Control measurement
- Information of participant
- Information about further results
  - Additional measurements
  - Ethically approved
    - In case of „bio-banking“

- www.umweltbundesamt.at
- www.eu-humanbiomonitoring.org
  - Available documents, ESBIO results
- www.umweltbundesamt.de
  - „Kinder Umwelt Survey“
- www.cdc.org
  - NHANES studies