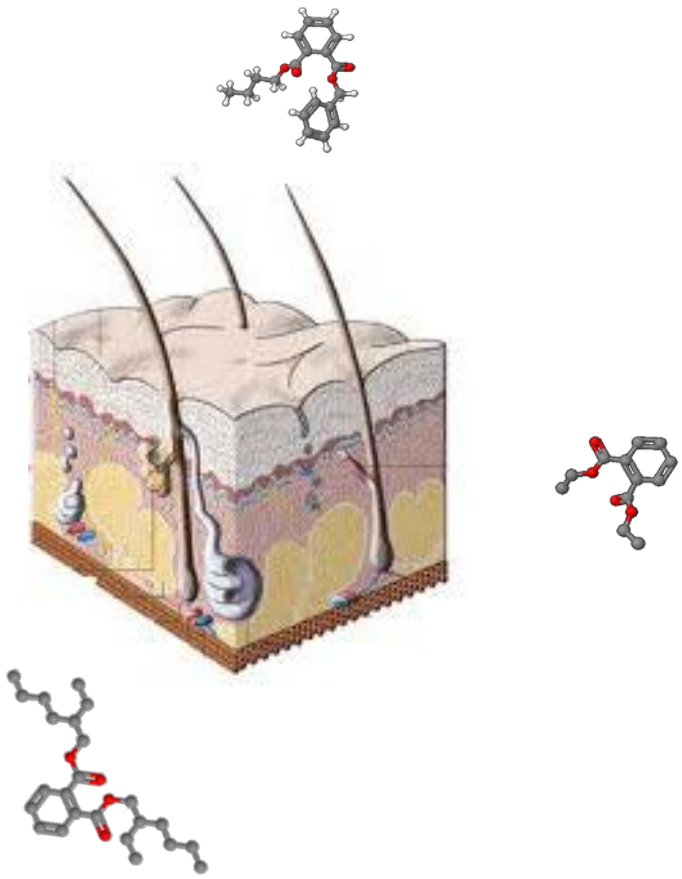
Dermal uptake of phthalates directly from air

Gabriel Bekö

International Centre for Indoor Environment and Energy
Department of Civil Engineering
Technical University of Denmark



You are what you…

…ingest, inhale, dermally absorb

Kawah Ijen vulcano sulfur mining - East Java

Numerous respiratory complaints

Life expectancy – 30 years

Is inhalation the only concern?

Dermal exposure

Asphalt roof workers

Dermal patch samples analyzed for PAHs (pyrene & BAP) and urine samples analyzed for 1-hydroxyprene

Significant dermal exposure *(McClean et al., 2007)*

Cashiers

Highest BPA exposure by occupation – dermal contact to receipts *(Braun et al., 2011)*

19-47% remains on hands after hand washing *(Fan et al., 2015)*

Dermal exposure

Tobacco farmers

Correlation between nicotine residue on hands and urinary excretion of cotinine & subjective symptoms.

(Kongtip et al., 2009)

Uptake from the surface of skin is well known

- Transdermal drug delivery (e.g., nicotine, estradiol, testosterone)
- Permethrin from impregnated military uniforms; naphthalene from stored clothing
- DEP and DnBP from creams applied to human skin (*Janjua et al., ES&T, 2007; Int J Androl, 2008*)

Uptake directly from air? YES for VOCs. ??? for SVOCs

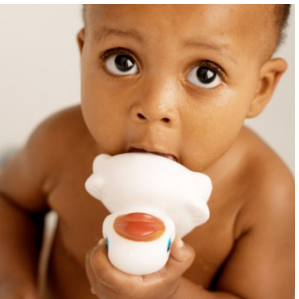
- Piotrowski (1967, 1971)
  - Subjects in chamber with **phenol**
  - Breathed *clean air*
  - Phenol (mg) found in urine
  - Similar results for **nitrobenzene**

- Bader et al. (2008)
  - Subjects in chamber with air containing **N-methyl-2-pyrrolidone (NMP)**
  - Dermal only exposure to NMP using face shield mask

- Measurements on skin (handwipes) and in the air indicate that SVOCs can go from air to skin. But what about the next step – from skin to blood? Modelling suggests this can be the case!

Phthalates

- Developmental and reproductive toxicants
- Indications of impact on: neurodevelopment, thyroid function, onset of puberty, behavioral development, obesity, respiratory problems

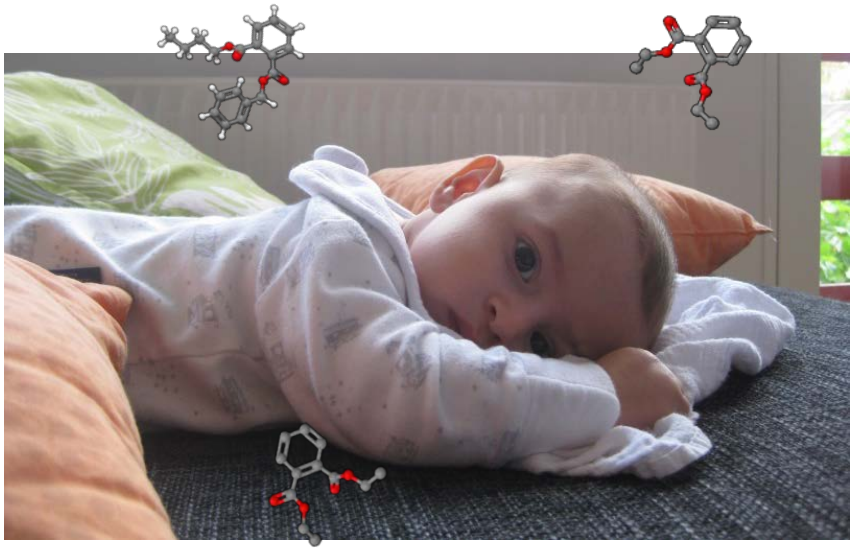






441 homes/children: Contribution of each pathway to total intake from urine

	DEP	DnBP	DiBP
Dust ingestion	0.5%	0.8%	1.2%
Inhalation	13%	1.6%	4.6%
Dermal-air	89%	14%	44%



Phthalates in skin and urine

Significant associations between the parent phthalate in handwipes and its monoester metabolite in urine for DiBP, DnBP, BBzP and DEHP

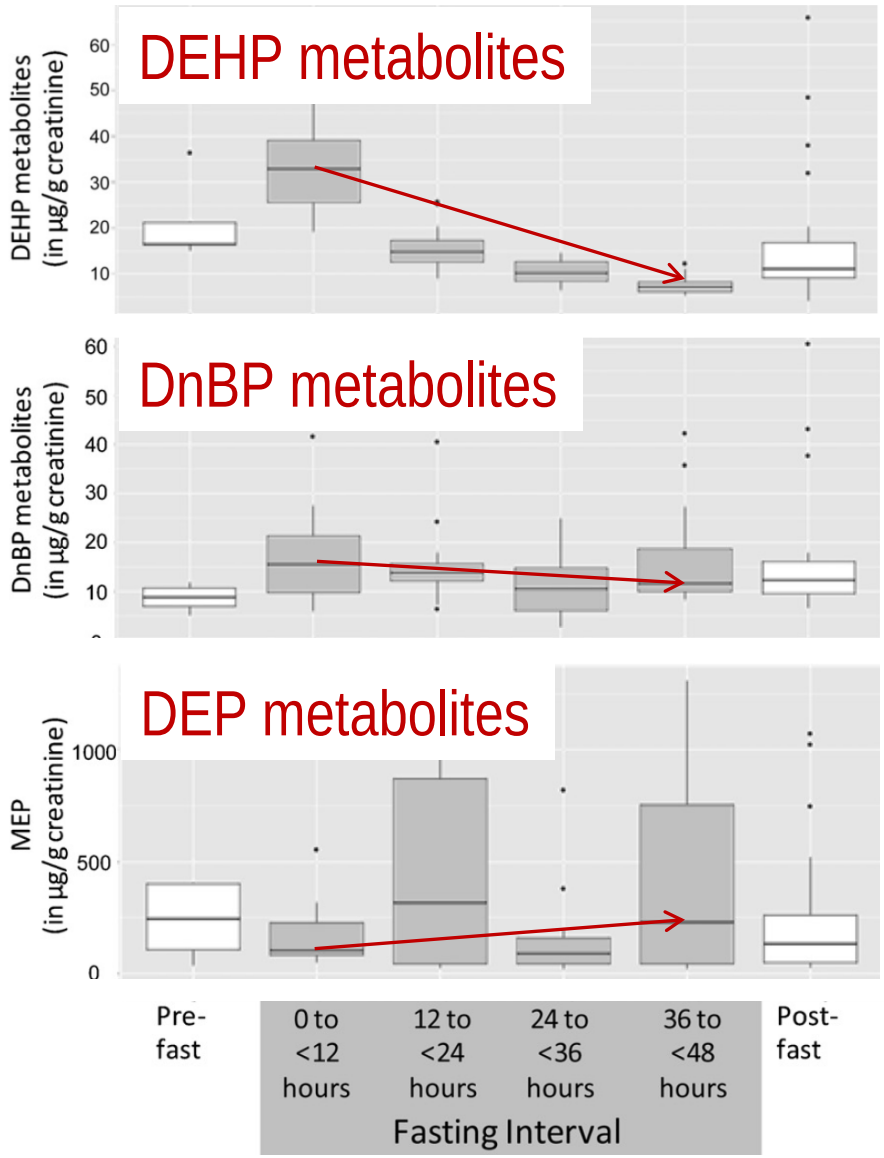
Gong et al. Indoor Air, 2015

Time to measure direct uptake!

Direct dermal uptake of DEP and DnBP in chamber experiments

- DEP is used as a solvent/carrier in many personal care products
- DnBP is used as a plasticizer for PVC and as a solvent/plasticizer in products such as nail polish
- DEP and DnBP are common in indoor air and indoor dust
- The metabolites of DEP and DnBP are often the most abundant manmade chemicals found in human urine samples
- Modeling suggests that dermal uptake, directly from the air, is an important exposure pathway for both
- Diet is not the dominant exposure pathway for either

Impact of 48 hr fast on metabolite levels



Rapid decrease

No effect

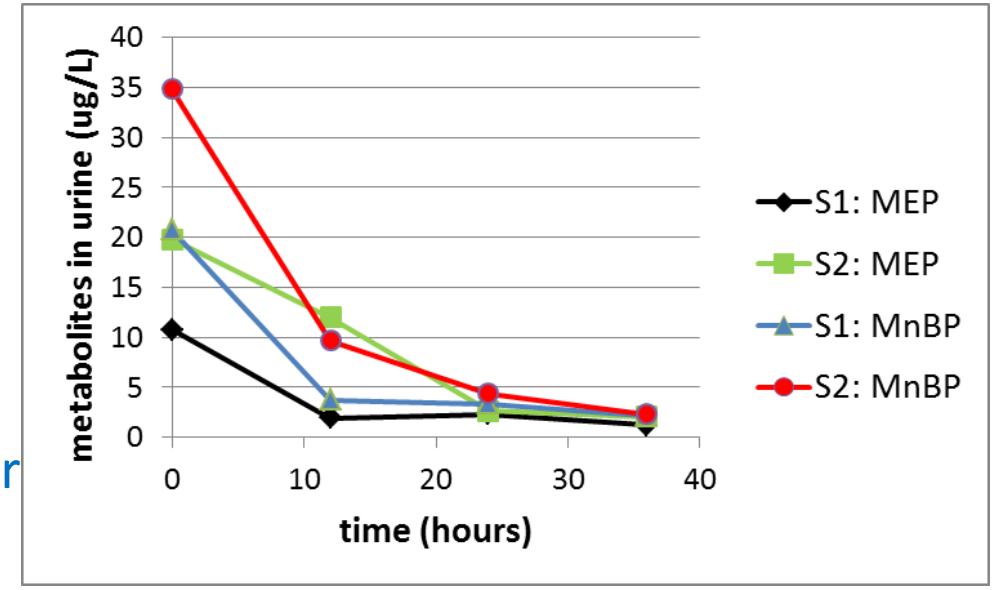
No effect

Koch et al., Int J Hyg Environ Health, 2013

Preliminary experiments

- DEP and DnBP levels in air needed to be > 100 µg/m^3 (typical indoor levels: DEP 0.1 to 0.6 µg/m^3; DnBP 0.3 – 1.4 µg/m^3)
- Latex paint doped with DEP & DnBP – Steady concentrations in air:
  ~250 µg/m^3 for DEP
  ~125 µg/m^3 for DnBP

- Reduction of background levels in our urine:
  - No use of personal care products
  - Restricted diet – **only**:
    - Tap water
    - Wasa "Sport"
    - Fruits with thick skins
- Urine samples from 8 subjects for 48 hours after beginning and continuing restrictions



Breathing arrangements
When the movies inspire science…

Dr. No

General van Dyke

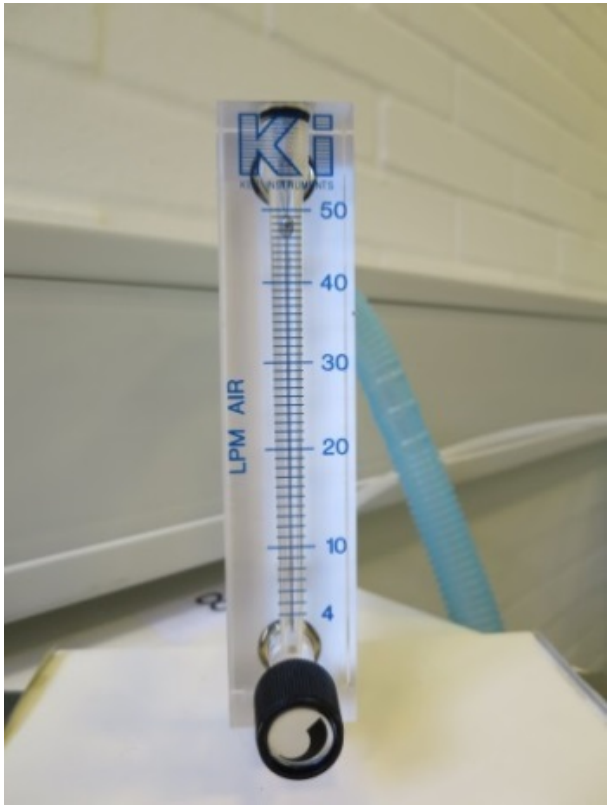
Alien??

Breathing arrangements

- To expose subject only dermally, we used “breathing hoods” used by Rigshospitalet (Copenhagen) in their hyperbaric oxygen chamber
- Checked the phthalate levels in breathing hood

Breathing arrangements

Outdoor air was compressed and filtered



Breathing air delivered at 48 liters/minute

Actual experiments

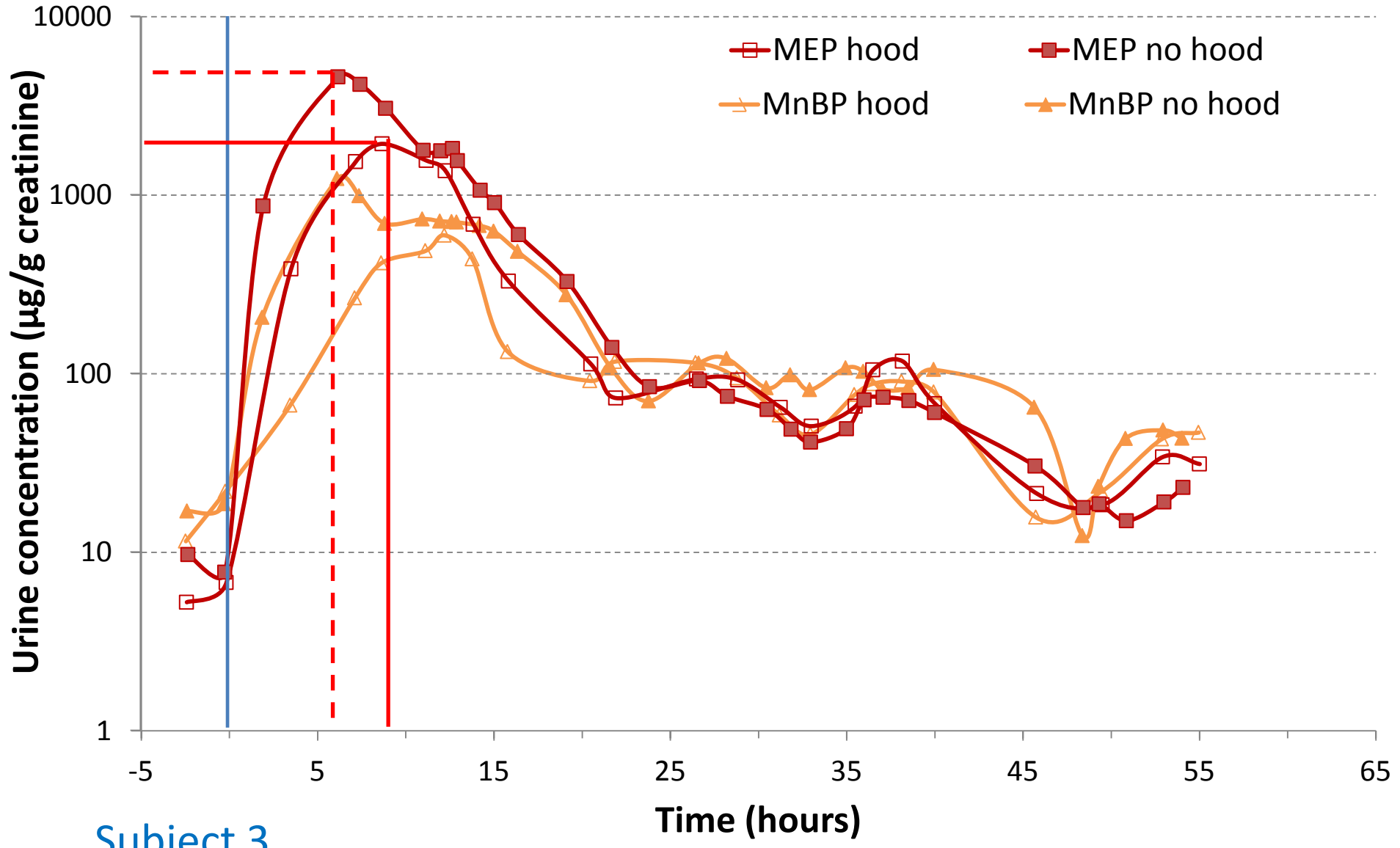
- 6 subjects
- 2 conditions
- 6 hours each (several days in between)
- Restricted diet and PCP use from 12h before until 48h after exposure
- 6+48 hours urine collection

Subjects in chamber during "dermal only" pathway experiments

Weighing urine samples

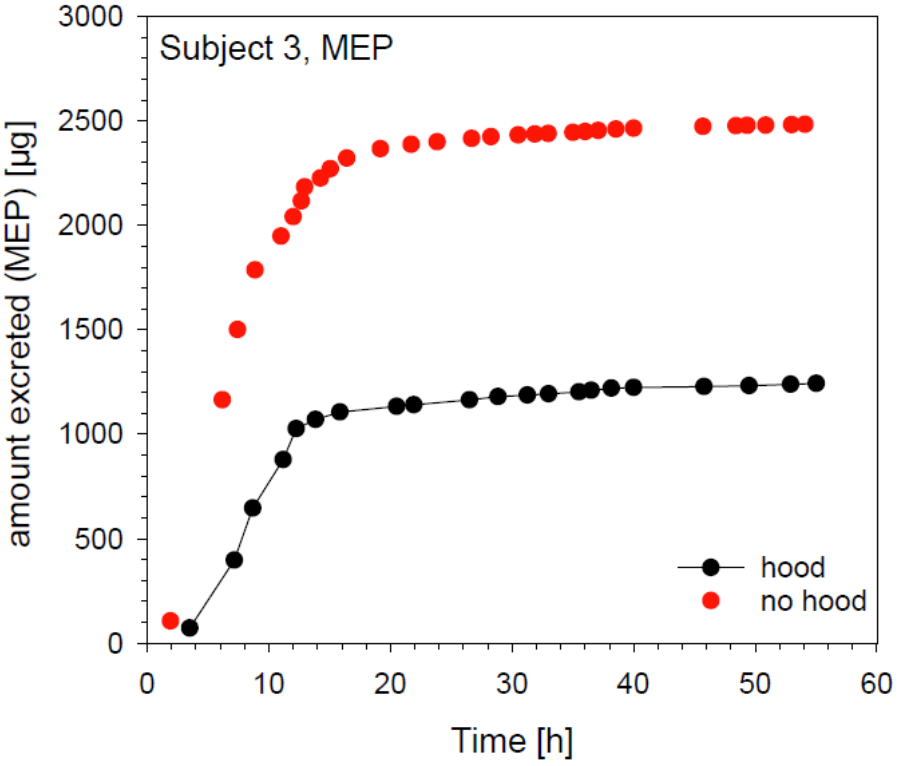
Urine samples in freezer before shipment to Germany for analysis

MEP & MnBP in urine vs. time



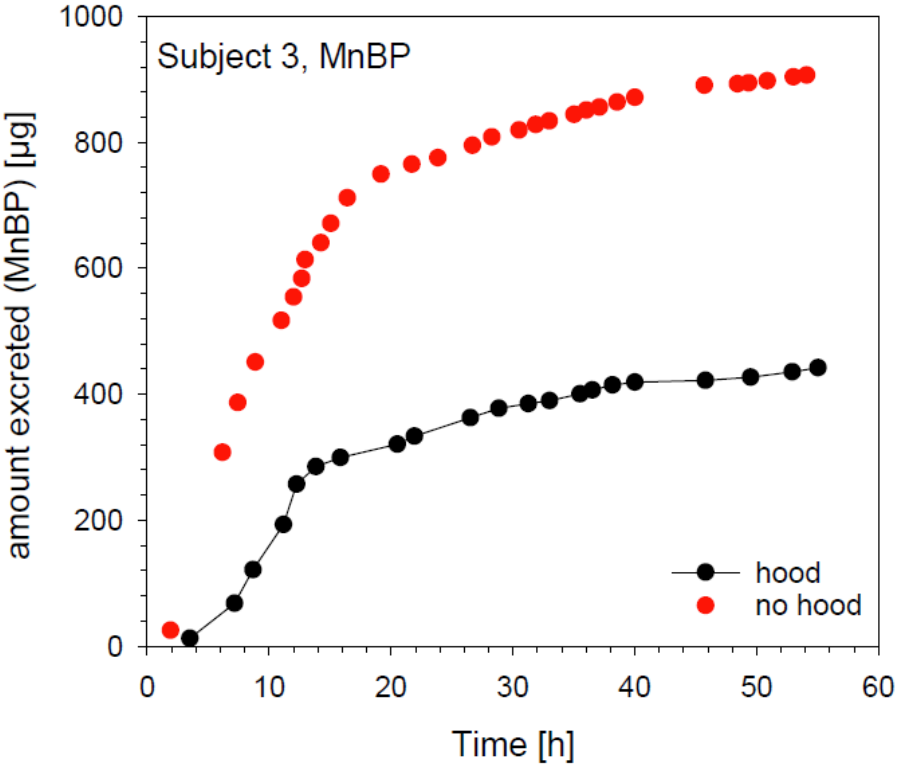
Subject 3

Net MEP & MnBP in urine vs. time



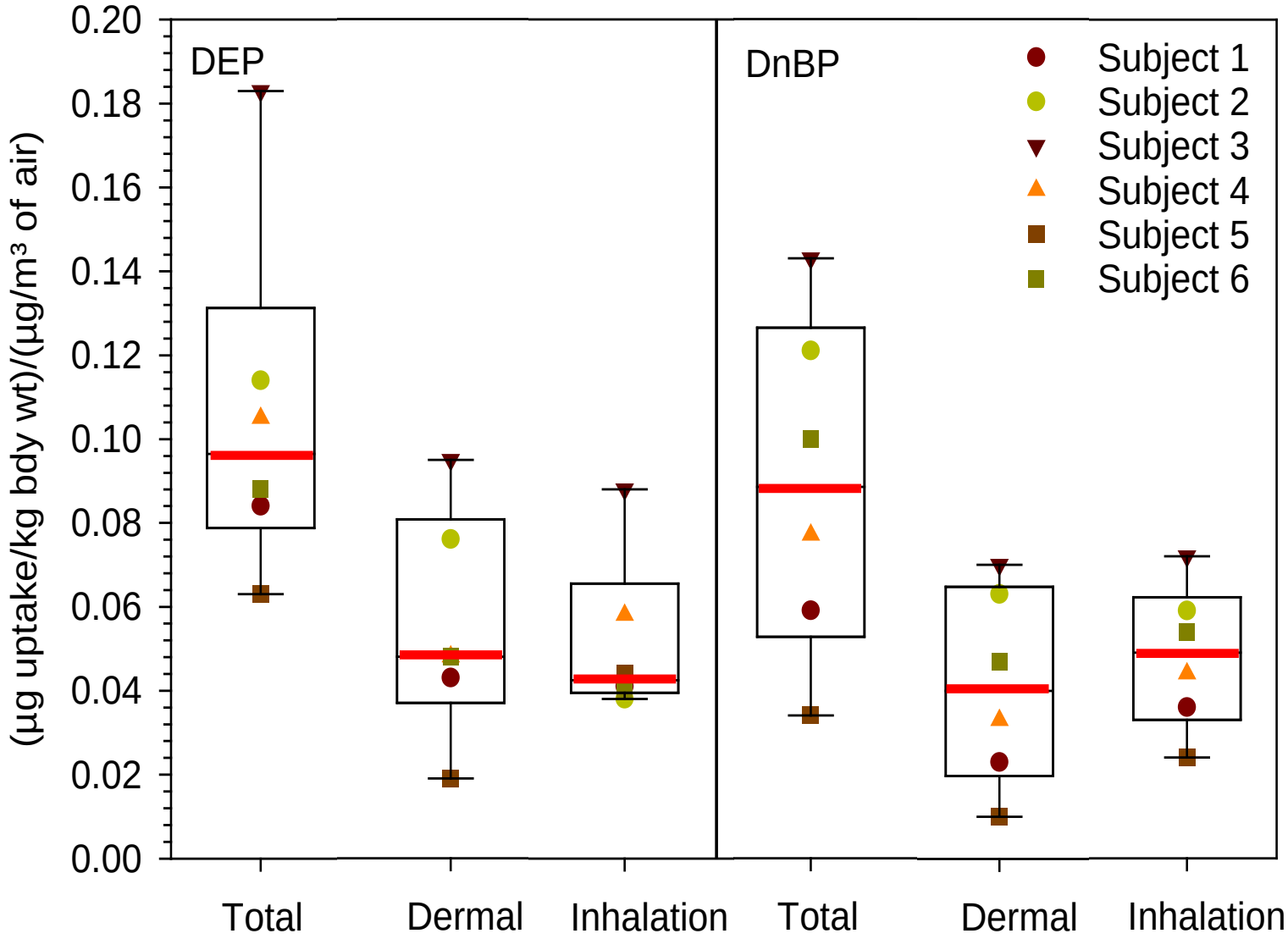
MEP, metabolite of DEP

MnBP, metabolite of DnBP



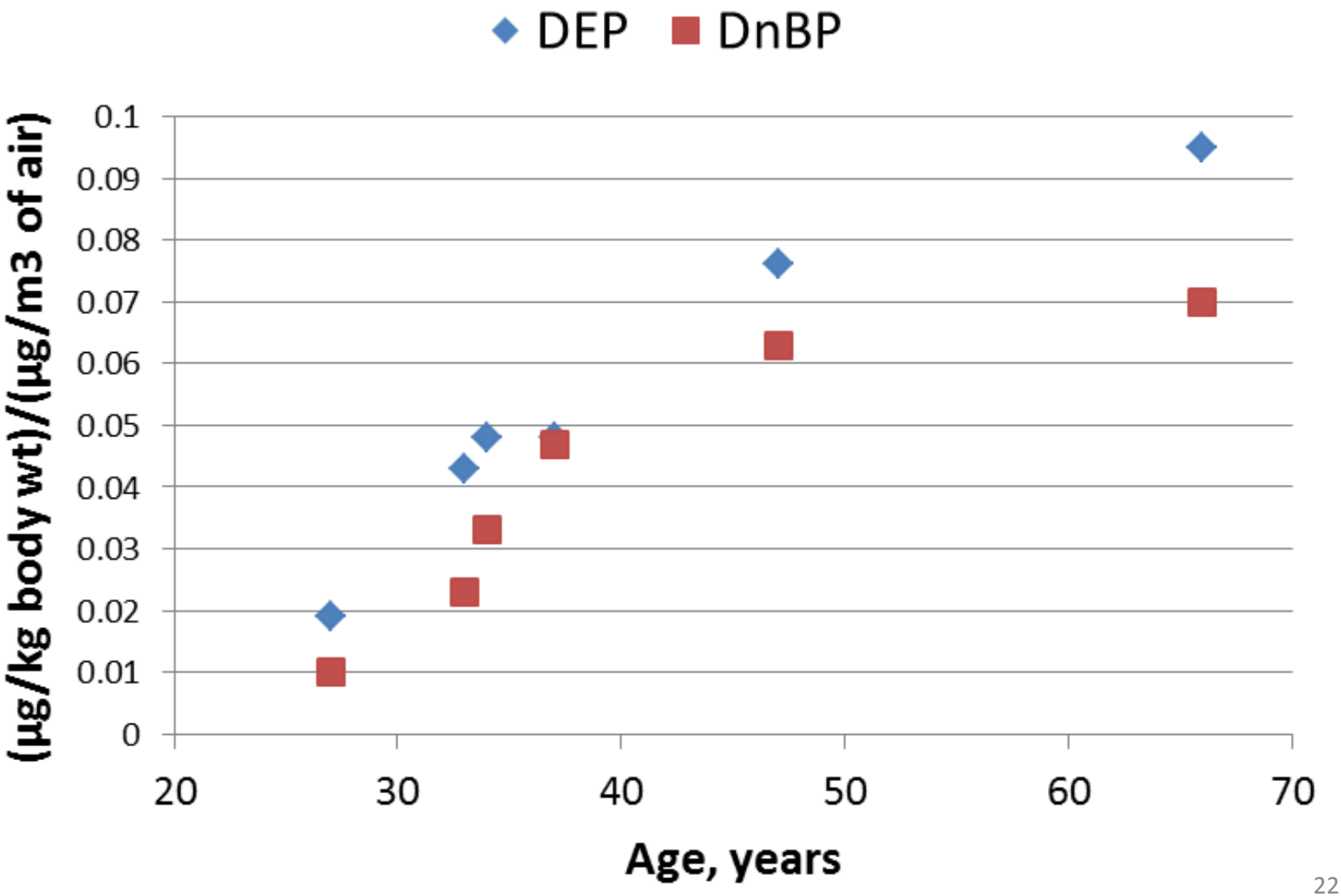
Weschler et al, Environ Health Perspect 2015

Net uptake normalized by air conc & weight

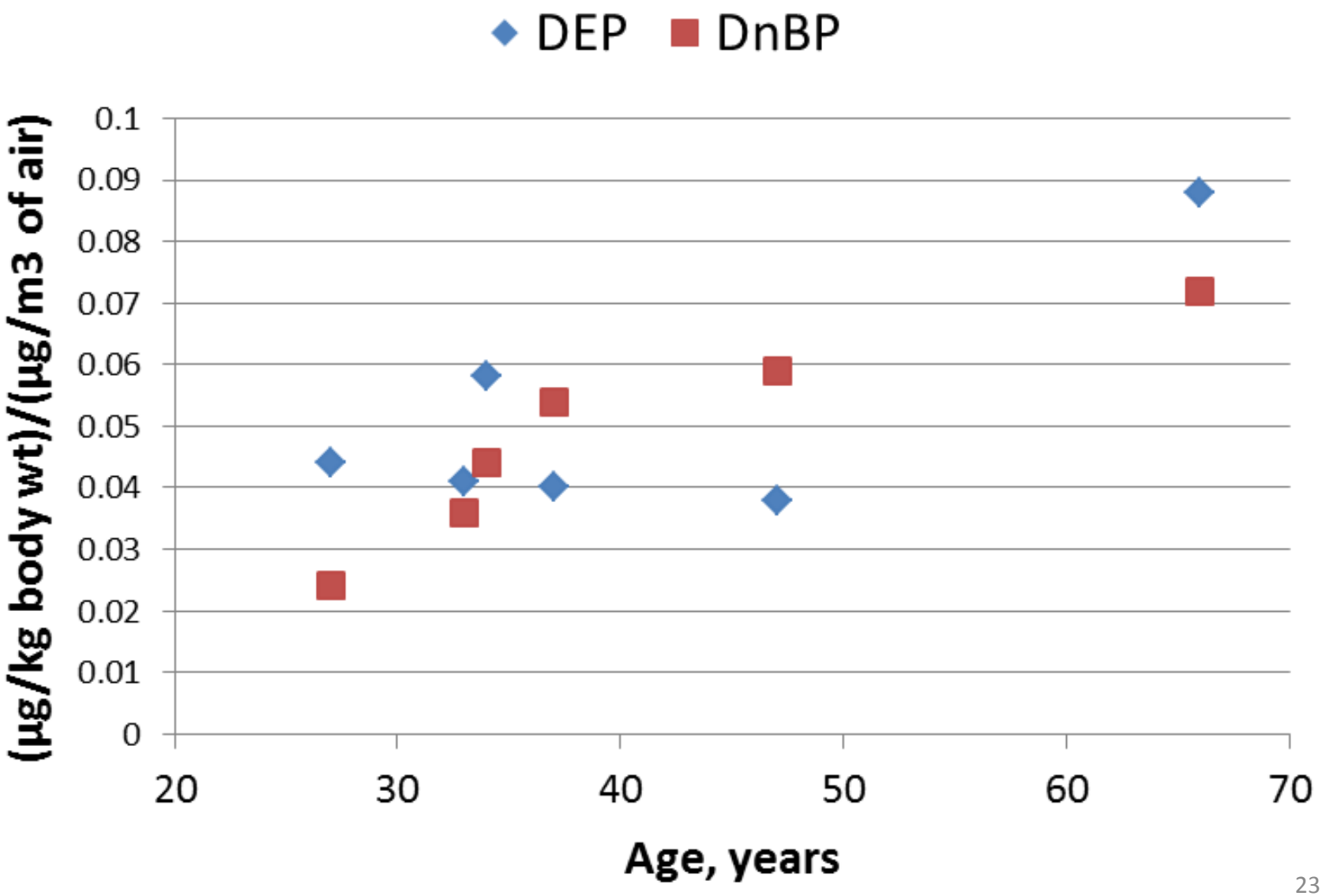


Weschler et al, Environ Health Perspect 2015

Net dermal uptake (normalized) vs. age



Net inhalation uptake (normalized) vs. age

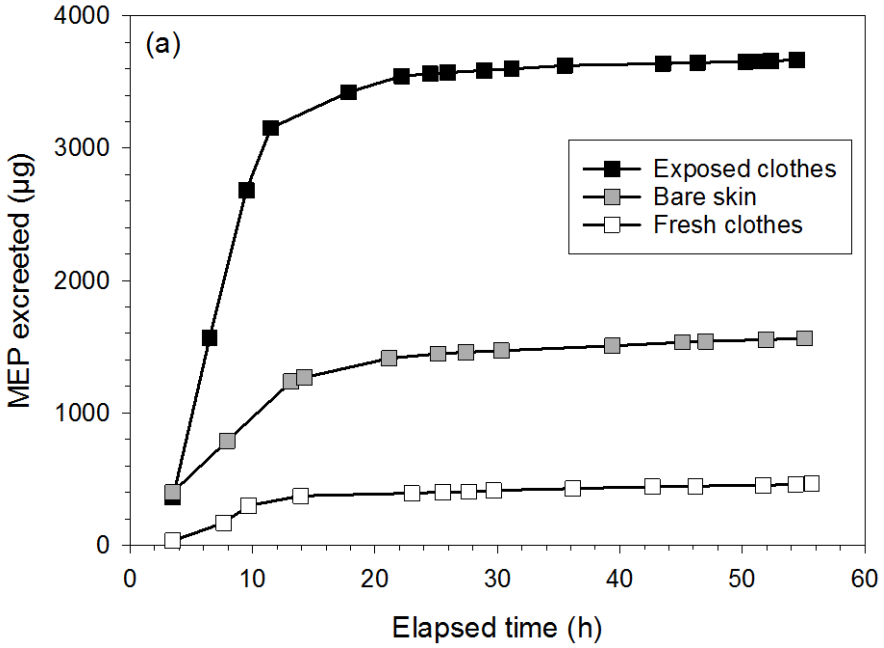


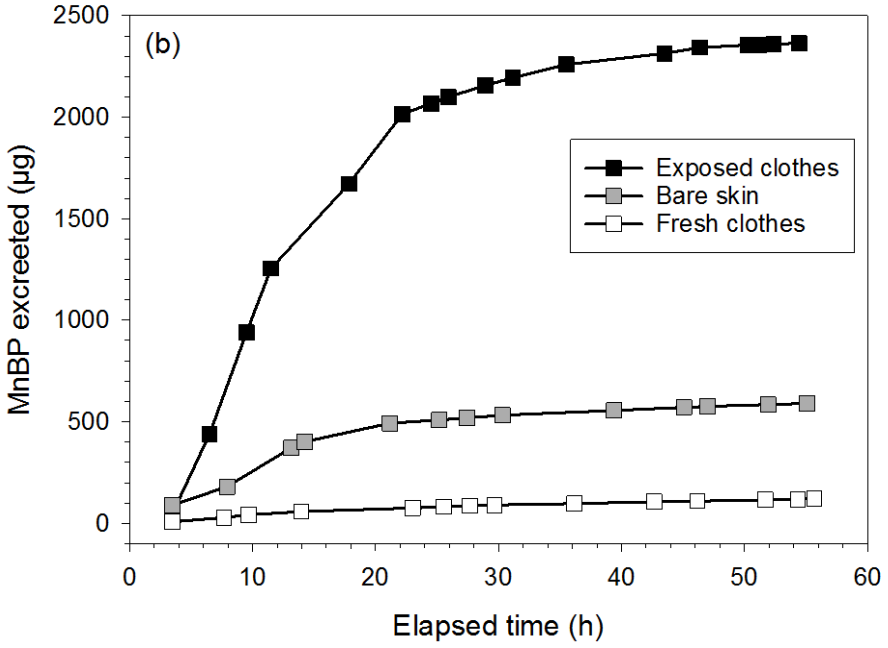
The role of clothing?

Freshly cleaned vs. exposed clothes

The role of clothing?

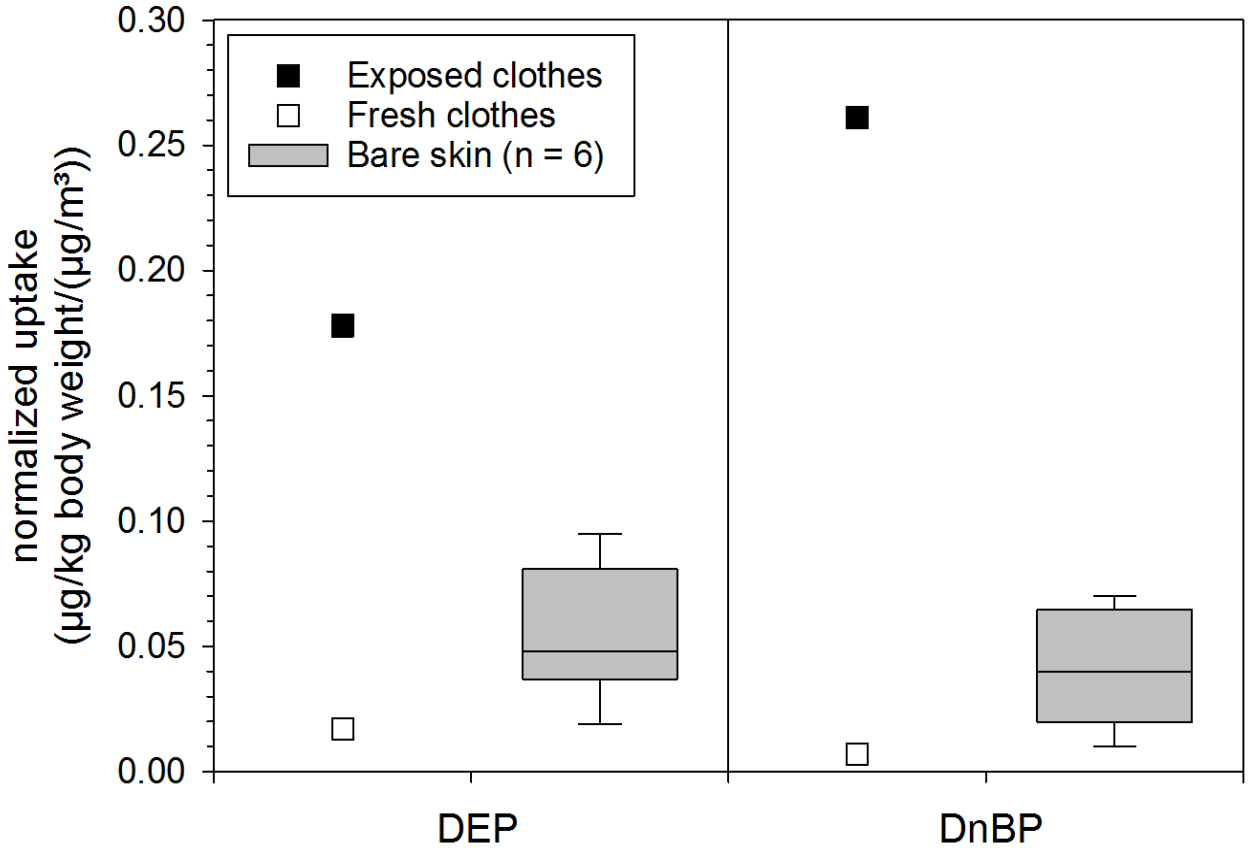
What got into him? Net MEP & MnBP in urine vs. time





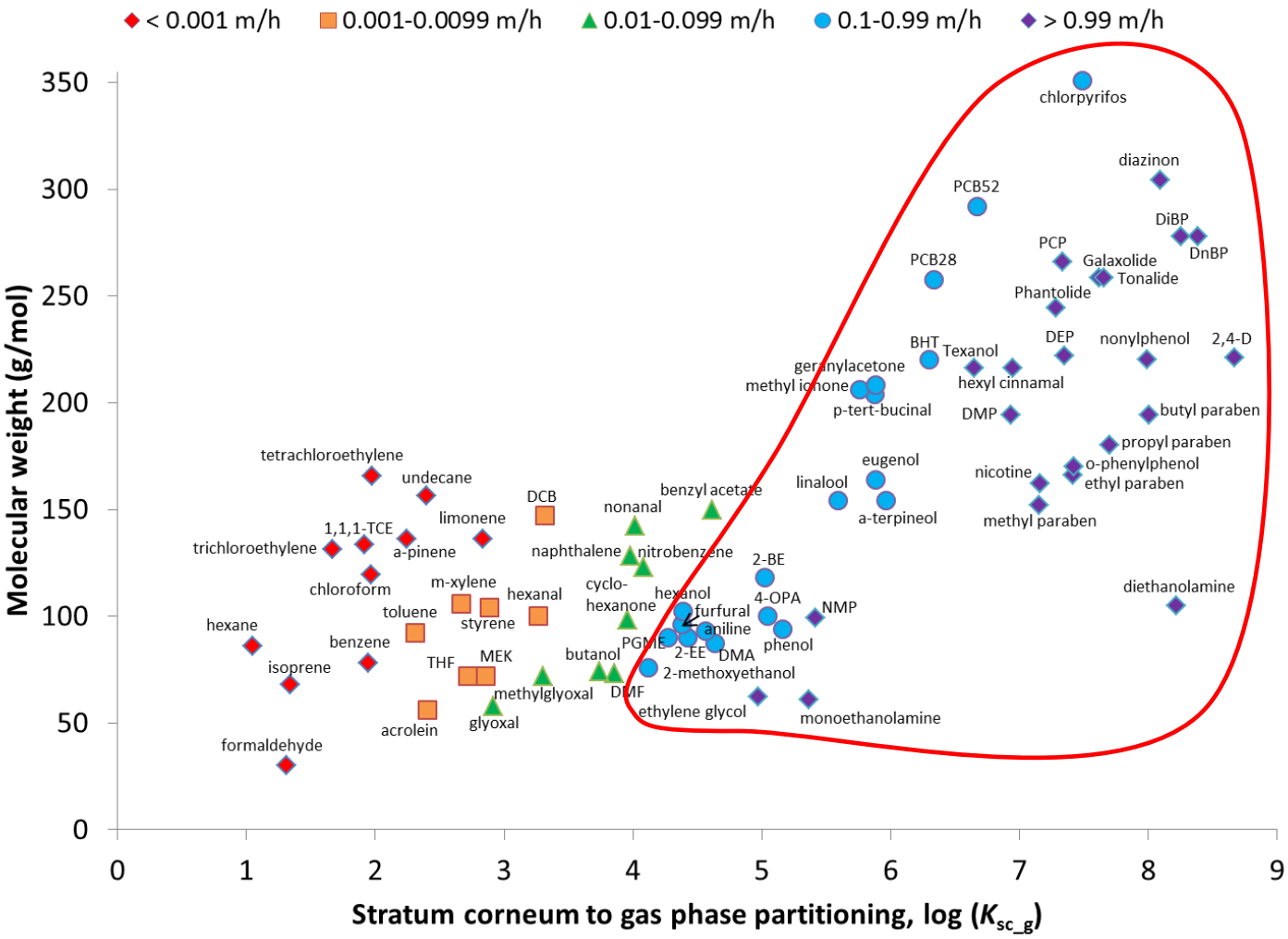
Morrison et al, J Expo Sci Environ Epidemiol 2015

Net uptake of DEP and DnBP normalized by air concentration & body weight



Morrison et al, J Expo Sci Environ Epidemiol 2015

Broader implications for dermal absorption from air

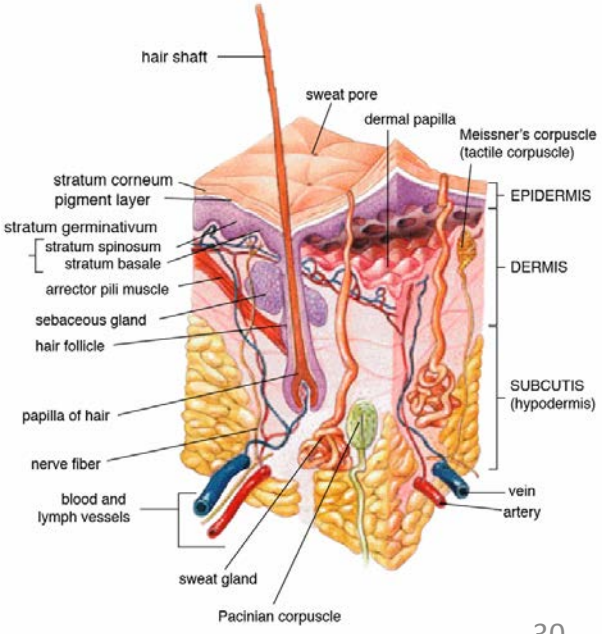


> thirty <u>common</u> indoor pollutants predicted to have dermal uptakes > co-occurring inhalation intake

Weschler and Nazaroff, Environ Sci Technol, 2014

Lots of questions to be answered

- What happens when we change environment (different air concentration) – steady state vs. dynamic conditions
- Effect of putting on clothes after chamber exposure (what does the clothes do to our skin surface lipids)
- Fabric properties, air gap, contact, air/cloth partitioning, time
- Bathing, bedding
- Complexity of air to skin to blood to urine processes (skin layers, composition, thickness, penetration, storage, metabolism…)
- …



Summary

- Dermal uptake, directly from air, is a meaningful exposure pathway for DEP and DnBP
- DEP uptake from air was roughly equal to inhalation intake; DnBP uptake from air was ~ 80% of inhalation intake (can be much higher in reality)
- Clean clothing can act as a barrier to dermal exposure from air
- Clothing that has absorbed chemicals can accelerate the dermal uptake of the absorbed chemicals
- We are exposed to “home pollutants” outside our home while wearing clothing that has absorbed home pollutants

Volunteers at their best

- Air sampling & analyses - Tunga Salthammer, Tobias Schripp (Fraunhofer WKI, Germany)
- Urine analyses - Holger Koch (Institute for Prevention and Occupational Medicine , Bochum, Germany)
- Glenn Morrison (Missouri Univ. of Science & Technology)

Glenn, Lulu & Tobias

Jørn and Geo