Triclosan exposure and allergy in Norwegian children

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Outline of the talk

• Background, triclosan
  – Sources and exposure
  – Potential health issues
  – Hypothesis for link to allergy

• Study design and methods

• Results
Triclosan, sources

• Synthetic antimicrobial agent
  – Permeates bacterial cell walls and targets multiple cytoplasmic and membrane sites, and disrupts lipid biosynthesis

• Used for more than 30 years
  – Sportswear, footwear, household cleaners, plastic coatings, and personal care products

• Personal care products accounted for 85% of the total volume of triclosan in Europe

The European Cosmetics Association, 2007
Triclosan (by weight %) in cosmetic products, Norway 2001

The Norwegian Food Control Authority, 2003
Triclosan in toothpaste

- 75% of the total amount of triclosan in personal care products was used in toothpaste (Norway, 2001)
- Toothpaste is defined as “rinse-off”-product
- Up to 36% of the triclosan dose from toothpaste was retained in the saliva and bacterial plaque for at least 8h

The Norwegian Food Control Authority, 2003
Gilbert et al, 1987
Triclosan, exposure

- Oral probably main route of exposure
- Triclosan also penetrates through human skin
- Breast milk, blood plasma, urine
Triclosan, metabolism

- **Controlled human exposure studies**
  - Half-life 11 hrs
  - Major fraction excreted within the first 24 hrs
  - 8 days to baseline levels
- **Strong plasma protein binding**
  - No unbound triclosan detected at either 1 or 10 µM concentrations, which could increase the effective half-life

Sandborgh-Englund et al, 2006
Rotroff et al, 2010
Urinary concentrations of triclosan in populations from different countries

- **Present study (Norway)** (10 yrs, n=623)
- **NHANES (U.S.)** (6-11 yrs, n=314)
- **NHANES (U.S.)** (12-19 yrs, n=715)
- **Mount Sinai (U.S.)** (girls, 6-8 yrs, n=1102)
- **China** (3-24 yrs, n=287)
- **Korea** (18-29 yrs, n=247)

Triclosan in µg/L (log scale)
In Vitro-to-In Vivo extrapolation of triclosan

- Human oral exposure estimates integrated with pharmacokinetic (PK) models taking into account human metabolic clearance and plasma protein binding
- Human oral exposure levels to triclosan is within the level where significant in vitro effects (disruption of cellular pathways) have been observed

Rotroff et al, 2010
Potential mechanisms and health issues

• Environment
  – Antibiotic resistance
  – Formation of carcinogenic by-products (dioxins)

• Human
  – Endocrine disruption (thyroid and sex hormones)
  – Skin irritation
  – Increasing rates of allergies

Dann and Hontela, 2011
Immune response and allergy development

- Our immune system may respond by different helper T cell responses, like Th1 and Th2
- Th1 is important in the defence against infections
- Th2 is responsible for the classic (IgE-mediated) allergic response
Immune response and allergy development

- Microbial exposure is important for maintaining the balance between a Th1 and Th2 immune response.
- Reduced microbial exposure could lead to a Th2-skewed immune response and more allergy (Hygiene hypothesis).
Triclosan and allergy development

Triclosan
• reduces the microbial diversity in the environment
• changes the biota in the oral mucosa
• down-regulate signals which activate the Th1 immune response

Yang et al, 2005; Barros et al, 2010
Triclosan and allergy, previous study

- NHANES 2003-2006
- Based on self-reported allergy
- Higher levels of triclosan associated with greater odds of ever having been diagnosed with allergies or hayfever in the < 18-year age group

Rees Clayton et al, 2011
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The Environment and Childhood Asthma Study

- Birth cohort study, Oslo
- Healthy term infants
- 1215 invited to 10-year follow-up
- 1019 children included (asthma-enriched due to inclusion of nested case-control study children)
- 540 children followed to 16 yrs of age
The Environment and Childhood Asthma Study

- Present study
  - Cross-sectional design from the 10-year follow-up 2002-2004
  - Includes 623 children (53% boys)
Exposure

- Triclosan analyzed by CDC, Atlanta
- 623 first morning voids 2002-2004
- Specific gravity
- 53% of the urine samples < limit of detection (LOD = 2.3 µg/L)
- Triclosan variable
  - Reference category: < LOD
  - Quartiles for concentrations > LOD
Outcomes

- **Allergic sensitization** by a positive skin prick test and/or serum IgE > 0.35 kU/L
  - both tested against a panel of 15 allergens (mites, animal dander, pollens, moulds and food)

- **Current rhinitis** (hayfever): symptoms of runny nose, blocked nose or sneezing (without having a cold) during the last 12 months
**Outcomes, cont**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N* (%) positive for the outcome</th>
</tr>
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<tbody>
<tr>
<td>Allergic sensitization</td>
<td>210 (34.9 %)</td>
</tr>
<tr>
<td>sIgE &gt; 0.35 kU/L</td>
<td>198 (32.8 %)</td>
</tr>
<tr>
<td>Skin prick test</td>
<td>164 (26.4 %)</td>
</tr>
<tr>
<td>Current rhinitis</td>
<td>163 (26.2 %)</td>
</tr>
<tr>
<td>Allergic sensitization and current rhinitis combined</td>
<td>103 (17.0 %)</td>
</tr>
</tbody>
</table>

All outcomes were more common among boys than girls

*at least 602 participants available for each outcome*
Statistics

- Logistic regression models adjusted for
  - specific gravity
  - gender
  - child’s BMI (age and gender corrected)
  - parental rhinitis
  - parental education level
  - household income
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Future directions

• Environment and Childhood Asthma study:
  – Association between triclosan exposure age 10 and increase in severity of allergy by age 16 (increase in SPT diameter and sIgE concentrations)
  – Quantify triclosan in urine samples collected at the 16-year follow-up
Summary

• Triclosan was detected in 47% of urine samples from Norwegian 10 year old children collected 2002-2004

• Results will be presented in a manuscript in the near future
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