Acrylonitrile exposure in the general population and emergency responders following a major train accident in Belgium: a human biomonitoring study


NVVA, 19/03/2015
Agenda

- Introduction
- Overview biomonitoring study
  - Data collection
  - Biomonitoring
- Results residents
- Results emergency workers
- Conclusions
Introduction

- May 4 2013 (2h30 AM): rail road accident in Wetteren: derailment of freight cars, explosion, and fire

- Three different substances in freight cars:
  - Butadiene
  - Triethylaluminium
  - Acrylonitrile (ACN)

- Water was used to extinguish the fire
Acrylonitrile metabolism

Acrylonitrile (=vinylcyanide, VCN)

- Conjugation
  - VCN-glutathione

- CYP2E1: oxidation
  - Cyanoethylene oxide (CEO)
    - Conjugation
      - CEO-glutathione
    - Epoxide hydrolase (EH)
      - Cyanide (CN)
        - Rhodanese
          - Thiocyanate (SCN)
            - Eliminated in the urine
Although acrylonitrile is heavier than air it can ascend in the sewer system of houses that have either no or a failing isolation from the main sewer system.
Introduction

• One resident was found deceased in his house with his dead dog
• One resident experienced cardiac arrest, but was successfully resuscitated
• One resident developed deep coma
• Around 200 residents presented at the emergency services of the surrounding hospitals
• More than 2000 residents were evacuated
• More than 2000 emergency workers were involved in the on-site management
Expert waarschuwt na treinramp:
Verhoogde kans op longkanker’

"Bloed laten invriezen als bewijs voor later"
Introduction

Human biomonitoring (HBM)
- Pressure from the media and public opinion “to do something”
- Pro
  - Every individual has the right to know whether he or she has been exposed
  - “Proof of exposure can be used in judicial/insurance matters when developing e.g. cancer”
  - Interesting from a scientific viewpoint
  - Information can be used in management of future incidents
- Con
  - Psychological impact
  - High cost
  - Exposure does not mean risk
Introduction

Decision to carry out HBM: Need for a fast study setup & start

Train accident  Decision HBM  Invitation to participate  Sampling residents  Sampling rescue workers  Sample Analysis

4/5  15/5  17/5  18-25/5  21/5-28/6
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Objective

To assess the human exposure to acrylonitrile (ACN) in the populations with highest suspected exposure, i.e. the residents of Wetteren and the persons that assisted professionally in the accident.
Data collection

**Sampling**: from May 18 till May 25 2013 for residents and May 21 till June 28 2013 for emergency responders

**Coordination**: FPS Health, Food Chain Safety and Environment + collaboration with the Province, the commune of Wetteren, the local general practitioners and occupational health services

**Ethics**: study protocol approved by UZ Ghent
Informed consent signed by all participants
Data collection

- **Blood**: N-2-cyanoethylvaline (CEV)
  → Biomarker for exposure to ACN

- **Urine**: cotinine
  → Biomarker for tobacco smoke exposure

- **Questionnaire**: Demographic variables, smoking status, sampling day and hour, detailed info about presence near the accident (time-space), symptoms.
Data collection

*N*-2-cyanoethylvaline (CEV)

- CEV is an adduct resulting from the binding of a metabolite of acrylonitrile to haemoglobin
- CEV is not toxic
- Highly sensitive and specific for exposure to acrylonitrile
- CEV level declines linearly to the background value during the lifespan of the circulating erythrocytes (126 days)
- Cigarette smoke contains acrylonitrile
Data collection

**Principle**: CEV adducts decrease linearly with time by 0.8% per day

**Formula**:  
Extrapolated CEV = measured CEV / (1 – t x 0.008)

Where ‘t’ = nb of days between accident and blood sampling

Ref: Bader et al., Toxicology Letter, 2006
CEV analyses

- Pretreatment at WIV-ISP → lysate of erythrocytes

- Because of need of substantial analyzing capacity
  → 3 German labs (G-Equas – additional interlaboratory comparison: comparable results among labs)

- Adduct dosimetry: modified Edman degradation
  (Von Sittert et al, 1986; Tornqvist et al, 1997)
Biomonitoring

Cotinine analyses
• online-SPE-UPLC-MS/-MS (De Cremer et al, 2013)

→ Definition of smoking status according to urinary cotinine levels and self-reported smoking status (questionnaire)

<table>
<thead>
<tr>
<th>Urinary cotinine (µg/L) + questionnaire</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 100 µg/L</td>
<td>Smoker</td>
</tr>
<tr>
<td>25 – 100 µg/L</td>
<td>Smoker</td>
</tr>
<tr>
<td>Self-reported current smokers</td>
<td>Smoker</td>
</tr>
<tr>
<td>Self-reported occasional smokers</td>
<td>Smoker</td>
</tr>
<tr>
<td>Self-reported ex-smokers</td>
<td>Non-Smoker</td>
</tr>
<tr>
<td>Self-reported non-smokers</td>
<td>Non-Smoker</td>
</tr>
<tr>
<td>&lt; 25 µg/L</td>
<td>Non-Smoker</td>
</tr>
</tbody>
</table>
Biomonitoring

Reference values CEV:

- Non-smokers: 10 pmol/g globin
- Smokers: 200 pmol/g globin

- Reference value is the 95\textsuperscript{e} percentile observed in the general population (not accidentally exposed to ACN).
- It correspond to the « upper limit » normally observed.
- Clearly more uncertain in smokers because CEV adduct levels may be very influenced by the tobacco consumption.
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Train accident

Railroad

Sewerage system

Prevailing wind directions at the moment of and in the days following the accident

Zone 1 (EZ1): 250m perimeter of the evacuation zone that was evacuated at night in the hours following the accident

Zone 2 (EZ2): streets parallel with the sewage system and downwind of the train accident that were evacuated later, i.e. in the days following the accident

Zone of ‘Controls’: the commune of Wetteren, EZ1 and EZ2 excluded
Results residents

The eligible population consisted of:

- **EZ1**: All the residents living within EZ1
- **EZ2**: All the residents living in EZ2 who presented at the emergency services
- **EZ2** (exit sign): 10% sample of the residents living in EZ2 who were evacuated, but did not present at the emergency services
- **OUT EZ**: All the residents of Wetteren living outside the EZ who presented at the emergency services

Children below the age of 10 were not included in the study.
# Results residents

<table>
<thead>
<tr>
<th></th>
<th>EZ1</th>
<th>EZ2</th>
<th>EZ2</th>
<th>OUT EZ</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligible (n)</td>
<td>40</td>
<td>99</td>
<td>219</td>
<td>116</td>
<td>474</td>
</tr>
<tr>
<td>Participants (n, %)</td>
<td>26  (65.0)</td>
<td>47  (47.5)</td>
<td>124 (56.6)</td>
<td>45  (38.8)</td>
<td>242 (51.1)</td>
</tr>
<tr>
<td>Age (years) Median (IQR)</td>
<td>48.5</td>
<td>47.0</td>
<td>48.0</td>
<td>34.0</td>
<td>45.0</td>
</tr>
<tr>
<td>Men n (%)</td>
<td>13  (50)</td>
<td>19  (40.4)</td>
<td>51  (41.1)</td>
<td>17  (37.8)</td>
<td>100 (41.3)</td>
</tr>
<tr>
<td>Non-smokers (%)</td>
<td>20  (76.9)</td>
<td>33  (70.2)</td>
<td>89  (71.8)</td>
<td>26  (57.8)</td>
<td>168 (69.4)</td>
</tr>
</tbody>
</table>
CEV(*) in the different EZ zones

<table>
<thead>
<tr>
<th>Non-smokers</th>
<th>EZ1 (n=20)</th>
<th>EZ2 (n=33)</th>
<th>EZ2 (n=89)</th>
<th>OUT EZ (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>13.7 (15.4)</td>
<td>662.8 (2325.0)</td>
<td>80.9 (317.0)</td>
<td>4.3 (3.3)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>9.9 (4.0-14.4)</td>
<td>8.0 (5.7-67.6)</td>
<td>6.8 (3.4-15.8)</td>
<td>3.0 (2.3-5.7)</td>
</tr>
<tr>
<td>P95</td>
<td>35.9</td>
<td>2760.6</td>
<td>339.5</td>
<td>8.2</td>
</tr>
<tr>
<td>Maximum</td>
<td>64.8</td>
<td>12614.8</td>
<td>2128.5</td>
<td>16.2</td>
</tr>
<tr>
<td>&gt;ref value n(%)†</td>
<td>10 (50.0)^</td>
<td>13 (39.3)$</td>
<td>30 (33.7)$</td>
<td>1 (4.2)*</td>
</tr>
</tbody>
</table>

‡10 pmol/g globin
* P value = 0.003; ^P value = 0.310 ; $ P value = 0.711
CEV concentrations extrapolated at the moment of the train accident (pmol/g globin)
Extrapolated CEV concentration $\leq 10$ pmol/g globin
Extrapolated CEV concentration $> 10$ pmol/g globin
Has been in the EZ at the moment of or in the days following the train accident
Extrapolated CEV concentrations of 4951 and 12615 pmol/g globin
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Results emergency workers

• Eligible population:
  All the emergency responders involved in the on-site management of the train accident from May 4 to May 13 (n=1054)

• Final study population for the analysis: n = 841
  = participants with blood CEV measures, urinary cotinine measures, and complete information from questionnaire and function.
Results emergency workers

→ 5 categories of functions:

1. fire-fighters
2. police
3. civil protection
4. army
5. others (including medical staff, journalists, wastewater management team, and soil remediation team)
### Results emergency workers

#### Characteristics of the study population (n = 841)

<table>
<thead>
<tr>
<th></th>
<th>fire-fighters</th>
<th>police</th>
<th>civil protection</th>
<th>army</th>
<th>others</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>450 (54%)</td>
<td>286 (34%)</td>
<td>35 (4.2%)</td>
<td>22 (2.6%)</td>
<td>48 (5.7%)</td>
<td>841</td>
</tr>
<tr>
<td>Men (n, %)</td>
<td>439 (97.6%)</td>
<td>224 (78.3%)</td>
<td>35 (100%)</td>
<td>21 (95.5%)</td>
<td>34 (70.8%)</td>
<td>753 (89.5%)</td>
</tr>
<tr>
<td>Age (median, IQR)</td>
<td>40.0 (33-46)</td>
<td>35.0 (29-44)</td>
<td>46.5 (41-49)</td>
<td>35.5 (31-49)</td>
<td>39.0 (31-46)</td>
<td>38.0 (32-46)</td>
</tr>
<tr>
<td>Smokers (n, %)</td>
<td>114 (25.3%)</td>
<td>67 (23.4%)</td>
<td>8 (22.9%)</td>
<td>5 (22.7%)</td>
<td>12 (25.0%)</td>
<td>206 (24.5%)</td>
</tr>
</tbody>
</table>
## Results emergency workers

Extrapolated CEV concentrations (pmol/g globin) in the non-smokers, by function (n = 635).

<table>
<thead>
<tr>
<th></th>
<th>fire-fighters</th>
<th>police</th>
<th>civil protection</th>
<th>army</th>
<th>others</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>336</td>
<td>219</td>
<td>27</td>
<td>17</td>
<td>36</td>
<td>635</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>4.4 (2.6-17)</td>
<td>2.9 (2.6-5.1)</td>
<td>15 (6.1-47)</td>
<td>2.6 (1.3-5.1)</td>
<td>5.1 (2.9-10)</td>
<td>3.2 (2.6-10)</td>
</tr>
<tr>
<td>95(^{th}) percentile</td>
<td>91</td>
<td>26</td>
<td>110</td>
<td>11</td>
<td>217</td>
<td>73</td>
</tr>
<tr>
<td>Maximum</td>
<td>452</td>
<td>117</td>
<td>147</td>
<td>11</td>
<td>379</td>
<td>452</td>
</tr>
<tr>
<td>N (%) &gt; ref value*</td>
<td>106 (31.5%)</td>
<td>29 (13.2%)</td>
<td>16 (59.3%)</td>
<td>1 (5.9%)</td>
<td>11 (30.6%)</td>
<td>163 (25.7%)</td>
</tr>
</tbody>
</table>

* 10 pmol/g globin
Results emergency workers

**Group «others»**: affiliation of the highest CEV values (non smokers)

<table>
<thead>
<tr>
<th>CEV_extrap.</th>
<th>AFFILIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>379,0</td>
<td>Medical staff</td>
</tr>
<tr>
<td>216,9</td>
<td>Aquafin + Ovam</td>
</tr>
<tr>
<td>127,6</td>
<td>Aquafin + Ovam</td>
</tr>
<tr>
<td>57,5</td>
<td>Aquafin</td>
</tr>
<tr>
<td>42,3</td>
<td>Aquafin + Ovam</td>
</tr>
<tr>
<td>36,2</td>
<td>ECOREM (veldwerkbegeleider bodemsanering)</td>
</tr>
<tr>
<td>33,5</td>
<td>Aquafin + Ovam</td>
</tr>
<tr>
<td>30,6</td>
<td>Journalist</td>
</tr>
<tr>
<td>15,5</td>
<td>Aquafin + Ovam</td>
</tr>
<tr>
<td>10,8</td>
<td>Aquafin + Ovam</td>
</tr>
</tbody>
</table>

→ 7 of the 10 highest values for this group are from Aquafin/Ovam
Conclusions

In the non-smoking residents, some clear patterns with regard to ACN exposure following the train accident were seen in function of the subgroups.

The non-smoking emergency responders had significantly lower concentrations as compared to the residents. Fire fighters and civil protection staff had higher CEV concentrations.

In smokers, no such patterns were observed. CEV adduct levels may be very influenced by the tobacco consumption.
Acknowledgments

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Thank you for your attention!