Acrylonitrile exposure assessment in the emergency responders following the train disaster in Wetteren

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In the night of 4 May 2013: train disaster in Belgium
The accident occurred in Wetteren, a village located in Flanders, at 15 km of the city of Gent and 45 km of Brussels.
Several tanks loaded with acrylonitrile (ACN) exploded, followed by a fire, and ACN leakage into the sewers. ACN vapours entered into the surrounding houses.
Residents were evacuated

- 1 deceased and 1 person in coma
- +/- 200 persons hospitalised
- More than 2000 persons evacuated
- More than 2000 emergency responders involved
Acrylonitrile

- Acrylonitrile (CH$_2$=CHCN) is a colourless, flammable and volatile liquid.
- It is a monomer that is used for the manufacture of synthetic rubber, resins, plastics, ...
- By combustion: release of cyanide (acute toxicity)
- Exposure may cause short-term irritation, nausea, vomiting, headache, dizziness and very high concentrations may cause even coma and death
- Long-term effects have been described in the literature only for chronic exposure. The substance is classified as possibly carcinogenic to humans (IARC Class 2B).
- Present in cigarette smoke
CH₂=CHCN (acrylonitrile) → CN⁻ → SCN⁻ → HEMOGLOBINE

Val-N—CH₂—CH₂CN (CyanoEthylValine, CEV) → CEMA, CHEMA, mercapturic acids
Human biomonitoring to ACN

1. Objective
2. Study population
3. CEV concentrations
4. Discriminating factors
5. Comparison with residents
Human biomonitoring to ACN

Objective:

To determine exposure to ACN and to assess discriminating factors for ACN exposure in the emergency responders involved in the on-site management of the train accident.
Human biomonitoring to ACN

1. Objective
2. Study population
3. CEV concentrations
4. Discriminating factors
5. Comparison with residents
Study population

- Eligible population:
  All the emergency responders involved in the on-site management of the train accident from May 4 to May 13

- Total number of participants: $n = 1054$

- Final study population: $n = 841$
  = participants with blood CEV measures, urinary cotinine measures, and complete information from questionnaire and function.
Data collection

- **Sampling**: from May 21 to June 28 2013, i.e. days 17 to 55 after the train accident – by the occupational health services
- **Ethics**: study protocol approved by UZ Ghent
  Informed consent signed by all participants
- **Collected**:
  - blood (for N-2-cyanoethylvaline, CEV)
  - Urine (for cotinine)
- **Specific questionnaire**:
  - detailed info about presence on site, day by day, but only till 10/05/2013; in 5 zones: <50m, 50-250m, 250-500m, 500-1000m, >1000m
  - question about use of respiratory protection
Five groups of function

Emergency responders were categorized in 5 groups:

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

#### 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>
Definition of smoking status

Definition of smoking status according to urinary cotinine levels and self-reported smoking status (questionnaire), in the emergency responders (n = 841)

<table>
<thead>
<tr>
<th>Urinary cotinine (µg/L) + questionnaire</th>
<th>Categorised as non-smokers</th>
<th>Categorised as smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 100 µg/L (n=198)</td>
<td>0</td>
<td>198</td>
</tr>
<tr>
<td>25 – 100 µg/L (n=15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-reported current smokers</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Self-reported occasional smokers</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Self-reported ex-smokers</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Self-reported non-smokers</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>&lt; 25 µg/L (n=628)</td>
<td>628</td>
<td>0</td>
</tr>
<tr>
<td>Total (n = 841)</td>
<td>635 (75.5%)</td>
<td>206 (24.5%)</td>
</tr>
</tbody>
</table>
Human biomonitoring to ACN

1. Objective
2. Study population
3. **CEV concentrations**
4. Discriminating factors
5. Comparison with residents
Measured CEV concentrations (pmol/g globin) in function of the sampling date in the emergency responders (n = 841).
Reference values for CEV

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

- Reference value is the 95<sup>e</sup> 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 are very influenced by the tobacco consumption.
Tab. 1: Konzentration an N-(2-Cyanoethyl)valin im Blut von Personen ohne beruflichen Kontakt zu Acrylamid

<table>
<thead>
<tr>
<th>Kollektiv</th>
<th>Konzentration an N-(2-Cyanoethyl)valin (pmol/g Globin)</th>
<th>Literatur</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (SD)</td>
<td>95. Perz.</td>
</tr>
<tr>
<td>Allgemeinbevölkerung</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NR (n=14)</td>
<td>4,9 (±1,9)*</td>
<td>k. A.</td>
</tr>
<tr>
<td>R (1 Packung/Tag) (n=18)</td>
<td>252 (±22)*</td>
<td>k. A.</td>
</tr>
<tr>
<td>R (2 Packungen/Tag) (n=14)</td>
<td>364 (±34)*</td>
<td>k. A.</td>
</tr>
<tr>
<td>NR (n=8)</td>
<td>&lt;2</td>
<td>&lt;2</td>
</tr>
<tr>
<td>R (n=10)</td>
<td>110</td>
<td>175</td>
</tr>
<tr>
<td>NR (n=18)</td>
<td>0,76*</td>
<td>k. A.</td>
</tr>
<tr>
<td>„Passivraucher“ (n=3)</td>
<td>1,1*</td>
<td></td>
</tr>
<tr>
<td>„Partyraucher“ (n=3)</td>
<td>8,6*</td>
<td></td>
</tr>
<tr>
<td>NR (n=24)</td>
<td>&lt;4</td>
<td>14</td>
</tr>
<tr>
<td>R (n=38)</td>
<td>131</td>
<td>241</td>
</tr>
<tr>
<td>NR (n=273)</td>
<td>&lt;4</td>
<td>7</td>
</tr>
<tr>
<td>R (n=97)</td>
<td>56</td>
<td>146</td>
</tr>
<tr>
<td>NR (n=591) **</td>
<td>&lt;4</td>
<td>&lt;4</td>
</tr>
<tr>
<td>„Passivraucher“ (n=98) **</td>
<td>&lt;4</td>
<td>&lt;4</td>
</tr>
<tr>
<td>R (n=144)</td>
<td>81</td>
<td>332</td>
</tr>
</tbody>
</table>

Abkürzungen: NR: Nichtraucher; R: Raucher; k. A.: keine Angabe
* Mittelwert
** Alter 18–65 Jahre
Measured CEV concentrations (pmol/g globin) in the emergency responders, by smoking status (n = 841).
Extrapolated CEV concentrations

- **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
Bader et al. (Toxicology Letter, 2006):

Fig. 2. Time-dependent decrease of ACN adducts in globin of a smoker (a) and a nonsmoker (b). Initial biomonitoring results are adjusted to 100%.
## CEV concentrations in non-smokers

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>95th percentile</td>
<td><strong>91</strong></td>
<td>26</td>
<td><strong>110</strong></td>
<td>11</td>
<td><strong>217</strong></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

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

logCEV extrapolated (pmol/g globin)

200 pmol/g globin

10 pmol/g globin

Others | Fire-fighters | Civil protection | Army | Police
Extrapolated CEV concentrations

**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
The extrapolation method used is adequate when the CEV background in the blood is negligible, i.e. in the case of non-smokers.

For the smokers, the use of this formula is more problematic because it does not take into account the background value due to tobacco smoking (value between 50 pmol/g globin and 300 pmol/g globin, depending on their tobacco consumption).

In the emergency responders, a precise evaluation of ACN exposure following the train accident is therefore not possible for smokers.

Extrapolated CEV data in smokers are given for information only.
Measured CEV concentrations (pmol/g globin) in the smokers, by function (n = 206).

<table>
<thead>
<tr>
<th>Function</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>114</td>
<td>67</td>
<td>8</td>
<td>5</td>
<td>12</td>
<td>206</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>156 (76-225)</td>
<td>105 (57-175)</td>
<td>153 (83-228)</td>
<td>132 (130-159)</td>
<td>100 (53-169)</td>
<td>140 (69-209)</td>
</tr>
<tr>
<td>95th percentile</td>
<td>403</td>
<td>282</td>
<td>331</td>
<td>323</td>
<td>284</td>
<td>342</td>
</tr>
<tr>
<td>Maximum</td>
<td>811</td>
<td>394</td>
<td>331</td>
<td>323</td>
<td>284</td>
<td>811</td>
</tr>
<tr>
<td>N (%) &gt; ref value*</td>
<td>38 (33.3%)</td>
<td>12 (17.9%)</td>
<td>2 (25%)</td>
<td>1 (20%)</td>
<td>2 (16.7%)</td>
<td>55 (26.7%)</td>
</tr>
</tbody>
</table>

* 200 pmol/g globin
### CEV concentrations in smokers

Comparison between measured and extrapolated CEV values, in non-smokers and smokers

<table>
<thead>
<tr>
<th></th>
<th>Measured CEV</th>
<th>Extrapolated CEV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-smokers (n=635)</td>
<td>Smokers (n=206)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>2,3 (2,0 - 8,1)</td>
<td>139,9 (69,4 – 209,4)</td>
</tr>
<tr>
<td>95th percentile</td>
<td>60,8</td>
<td>342,0</td>
</tr>
<tr>
<td>Maximum</td>
<td>354,6</td>
<td>811,3</td>
</tr>
<tr>
<td>Nb &gt; ref value</td>
<td>145 (22,8 %)</td>
<td>55 (26,7 %)</td>
</tr>
<tr>
<td>Nb &gt; 2x ref value</td>
<td>93 (14,6 %)</td>
<td>6 (2,9 %)</td>
</tr>
</tbody>
</table>
Human biomonitoring to ACN

1. Objective
2. Study population
3. CEV concentrations
4. **Discriminating factors**
5. Comparison with residents
Determinants of CEV levels: CART analysis

Discriminating factors for CEV concentrations were identified by the Classification & Regression Tree (CART) methodology\(^1\).

The CART is a nonparametric technique that incorporates two different types of tree-based methods: classification trees and regression trees.

CART can use the same predictor variable in different places in the tree, allowing for complex interdependencies between different predictor variables to unfold.

CART analysis

• **Predictor variables:**
  - gender; age; smoking status;
  - occupational function (five categories);
  - use of respiratory protection per day between May 4-10;
  - the zone of presence on-site in the night of the train accident and by day between May 4-10;
  - the cumulative number of days in each of the three predefined zones between May 4-10;
  - and the closest zone of presence on-site between May 4-10.

• **Response variable:** (log-transformed) extrapolated CEV concentrations
CART results
(in non-smokers, n=635)

- function
  - police or army
    - (p < 0.001)
  - fire-fighters, civil protection, others
    - (p < 0.001)
- present < 50 m
  - (p < 0.001)
- Nb of days in 50-250 m
  - ≤ 1 (p=0.019)
  - > 1
- Nb of days > 250 m
  - ≤ 5 (p = 0.021)
  - > 5

- Nb of days < 50 m
  - ≤ 2 (p = 0.013)
  - > 2

- CERV (pmol/g globin)
  - n = 219
  - n = 181
  - n = 24
  - n = 55
  - n = 133
  - n = 23
Human biomonitoring to ACN

1. Objective
2. Study population
3. CEV concentrations
4. Discriminating factors
5. Comparison with residents
Comparison with residents: CEV distribution

Overexposure in emergency responders is limited as compared to the residents and remains within the margins as expected in a smoking population.
Comparison with residents: profile of exposure

**In residents:** exposure in the direct vicinity of the site + exposure via the sewerage system. (ref: De Smedt et al. 2014)

**In emergency responders:**

Results suggest also the potential influence of the sewerage system:

- Higher CEV levels in firefighters and civil protection workers.
- Higher CEV levels in group ‘other’: majority are from wastewater management staff.
General conclusions

• An accident-related increased exposure to ACN was found in emergency responders present on-site:
  26% > reference value (non-smokers)
• Three functions with increased exposures: fire-fighters, civil protection, and « others » (including wastewater/soil remediation staffs).
• Exposure of emergency responders is limited in comparison with residents and remains within the marges as expected in a smoking population.
• Profile of exposure: in the direct vicinity of the site of the train derailment + via the sewerage system.
Acknowledgements

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  • For funding
  • Volunteers of B-Fast team

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