INTERESTING TOXICOLOGY CASES

Bruce J. Kelman, PhD, DABT, ATS, Registered Toxicologist (UK and EUROPEAN Registries)
Outline

• Causation analysis performed by toxicologists

• Difference between differential diagnosis and differential etiology

• Forensic case 1 (Air traffic control tower)

• Forensic case 2 (Coaxial cable-induced illness)

• Construction defect (Seattle Public Schools)
Did exposure to a chemical cause this injury?

Causation paradigm

TOXICOLOGIST
Toxicologist causation

Was chemical present?
Toxicologist causation

Can chemical \textit{cause} the effect (at any dose)?
Toxicologist causation

Was exposure sufficiently large and long to cause the effect?
Toxicologist causation

Did effects occur within an *appropriate time frame* of exposure?
Toxicologist causation

What are alternative causes of the effect?
Specific causation evaluation

Was chemical present?

Can chemical cause the effect (at any dose)?

Was exposure sufficiently large and long to cause the effect?

Did effects occur within an appropriate time frame of exposure?

What are alternative causes of the effect?
PHYSICIANS
Differential diagnosis/etiology

- Differential diagnosis
  - Identifies a set of diseases or illnesses responsible for the patient’s symptoms
  - Part of (but different than) causation

- Differential etiology
  - Identifies causal factors involved in an individual’s disease or illness
Differential diagnosis/etiology

- Symptom presentation
- Evaluate patient/signs
- Conduct and interpret diagnostic testing
- Set of diseases considered
- Rule out diseases or injuries
INTERESTING TOXICOLOGY CASES
Interesting cases to be shared today

- Forensic cases (2)
- Seattle Public Schools construction defect
Air Traffic Control Tower

Case #1
Case #1: Air Traffic Control Tower

- Air traffic controller claimed injury from exposure to vapor from HVAC cleaner
Exposure claim

- Vapors drawn into HVAC system and distributed to area where the subject worked
- Subject smelled a slight pungent orange/lemon-type scented odor for ~10 min before leaving area
- Reported nausea, dizziness, facial and hand numbness immediately following exposure
Health claims

- difficulty sleeping
- fatigue
- memory & concentration difficulties
- lightheadedness
- dizziness
- headaches
- disorientation
- delayed speech/word finding
- stuttering
- ↑ sensitivity to smells
- metallic dysgeusia

- facial numbness
- tongue numbness
- jaw paralysis
- extremity numbness
- ↓ left-side corneal reflex
- palpitations
- hyperventilation
- ↑ blood pressure
- breathing difficulty with chest tightness
- nausea
- chills
Medical records

<table>
<thead>
<tr>
<th>Day</th>
<th>Subjective complaints</th>
<th>Objective Findings</th>
<th>Diagnosis/Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Dizziness</td>
<td>Unremarkable</td>
<td>Dx: “Chemical inhalation”</td>
</tr>
<tr>
<td></td>
<td>Face &amp; hand numbness</td>
<td></td>
<td>“…the condition found was caused or aggravated by the employment activity described.”</td>
</tr>
<tr>
<td>5</td>
<td>Metallic taste</td>
<td>Persistent normal objective findings</td>
<td>Dx: “Trichloroethylene exposure”</td>
</tr>
<tr>
<td></td>
<td>Intermittent dizziness</td>
<td>Unremarkable neurological exam</td>
<td>Causation: “It appears this is consistent with trichloroethylene exposure, which is industrial.”</td>
</tr>
<tr>
<td></td>
<td>Somewhat weak and wobbly</td>
<td>[except ↓sensation in left trigeminal area, a subjective determination]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slight numbness below left eye</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Medical records

<table>
<thead>
<tr>
<th>Day</th>
<th>Subjective complaints</th>
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</thead>
<tbody>
<tr>
<td>132</td>
<td>Short term memory issue</td>
<td>Neuropsychological evaluation</td>
<td>“Based on my testing, it appears that there is some legitimate organic deficiency, but at the very high end of the cognitive spectrum. However, the very fact that she sees herself as any less competent than she is accustomed to being produces a tremendous secondary shock which exacerbates the reality of her situation.”</td>
</tr>
<tr>
<td></td>
<td>Lack of concentration</td>
<td></td>
<td>Psychotherapy</td>
</tr>
<tr>
<td></td>
<td>Lack of energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Difficulty sleeping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>246</td>
<td>Slight numbness around left eye, left side of tongue and lips</td>
<td>Unremarkable, except: Well-healed, multiple surgical scars above left wrist from prior surgery</td>
<td>“Adequate evidence does not presently exist to support the conclusion of direct work related causation.”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slight subjective sensation in lateral 2 fingers</td>
<td>“There is no subjective finding to substantiate this diagnosis [trigeminal neurologic related to TCE exposure].”</td>
</tr>
</tbody>
</table>
## Medical records

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<tbody>
<tr>
<td>568</td>
<td>Cognitive, concentration and memory Sx. Occasional minor back pain flares. Numbness of face and tongue.</td>
<td>Unremarkable, except: Decreased sensation to touch of left mid face.</td>
<td>“…her symptoms in the short period of time after the incident were more consistent with anxiety and hyperventilation.” “There is a distinctly functional (psychologically mediated, hypersomatic) flavor to her clinical presentation. Her current presentation of persistent cognitive symptoms is not related to any organic effects of the events and has no toxic basis.”</td>
</tr>
</tbody>
</table>
Specific causation evaluation (toxicology)

- Was chemical present?
- Can chemical cause the effect (at any dose)?
- Was exposure sufficiently large and long to cause the effect?
- Did effects occur within an appropriate time frame of exposure?
- What are alternative causes of the effect?
Was the chemical present?

- Trichloroethylene (CAS #79-01-6)
- Limonene
Is the chemical capable of producing claimed health effects?

- difficulty sleeping
- fatigue
- memory & concentration difficulties
- lightheadedness
- dizziness
- headaches
- disorientation
- delayed speech/word finding
- stuttering
- ↑ sensitivity to smells
- metallic dysgeusia

- facial numbness
- tongue numbness
- jaw paralysis
- extremity numbness
- ↓ left-side corneal reflex
- palpitations
- hyperventilation
- ↑ blood pressure
- breathing difficulty with chest tightness
- nausea
- chills

Green bullet indicates symptoms consistent with acute inhalation TCE-exposure (ATSDR, 2007).
Was exposure sufficient to cause claimed health effects?

- Exposure assessment:
  - **Model** upper limit of exposure using output of aerosolized cleaner (measured mass difference per 3 sec)
  - **Upper limit** of exposure in office was 5.3 ppm
Was exposure sufficient to cause claimed health effects?

<table>
<thead>
<tr>
<th>Trichloroethylene (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Odor threshold, ≥0.5 ppm</td>
</tr>
<tr>
<td>Odor detection, 52 ppm</td>
</tr>
<tr>
<td>Mild eye irritation, 200 ppm</td>
</tr>
<tr>
<td>OSHA ceiling, 200 ppm</td>
</tr>
<tr>
<td>CAL STEL, 200 ppm</td>
</tr>
<tr>
<td>ACGIH STEL, 25 ppm</td>
</tr>
<tr>
<td>OSHA PEL (8h TWA), 100 ppm</td>
</tr>
<tr>
<td>Cal PEL (8h TWA), 25 ppm</td>
</tr>
<tr>
<td>NIOSH REL (10h TWA), 25 ppm</td>
</tr>
<tr>
<td>ACGIH TLV (8h), 10 ppm</td>
</tr>
</tbody>
</table>
Did effects occur within an appropriate time frame?

- Symptoms started after reading MSDS
- Symptoms were progressively worse over time
Alternative explanations

<table>
<thead>
<tr>
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| 132  | Short term memory issue        | Neuropsychological evaluation     | “Based on my testing, it appears that there is some legitimate organic deficiency, but at the very high end of the cognitive spectrum. However, the very fact that she sees herself as any less competent than she is accustomed to being produces a tremendous secondary shock which exacerbates the reality of her situation.”  

**Psychotherapy**
Alternative explanations

- Idiopathic environmental intolerances (IEI)
  - an acquired disorder characterized by recurrent nonspecific symptoms that occur in response to exposure to many, often odorous, chemically unrelated compounds at doses well below the levels shown to cause harmful effects
  - *General consensus by the scientific community*:* the toxigenic theory of IEI is unproved and unsubstantiated and more likely to be psychogenic in origin*

*American Academy of Allergy Asthma and Immunology; American College of Occupational and Environmental Medicine; American College of Physicians American Medical Association; World Health Organization*
Coaxial Cable-Induced Illness

Case #2
Case #2: Coaxial Cable-Induced Illness

- Two telecommunication workers running cable claimed injury from chemicals off-gassing from coaxial cable.
Exposure claim

- A “smell” emanated from new cable they were installing in an office building
- Telecommunication workers claimed exposure to and injury from compounds off-gassing from the cable
Health claims – Employee #1

- **Respiratory tract effects**
  - Nasal irritation, congestion; runny nose; sinus congestion; sneezing
  - Throat soreness, tightness, irritation
  - Hoarseness
  - Chest congestion & tightness
  - Cough and sputum
  - Breathing difficulty
  - Shortness of breathing from physical exertion

- **Neurological effects**
  - Headache, disorientation, concentration difficulty, weakness, fatigue, deterioration of speech pattern

- **Ocular effects**
  - Dryness, irritation, redness, soreness

- **Other symptoms**
  - Flu-, cold-, or arthritis-like
  - Loss of appetite
  - Loss of thyroid organ
  - Nausea when exposed to other solvents
  - Stiffness and achiness of muscles
Health claims – Employee #2

- **Respiratory tract effects**
  - Nasal burning, irritation
  - Throat soreness
  - Hoarseness
  - Chest tightness
  - Cough
  - Breathing difficulty
  - Shortness of breathing from physical exertion

- **Ocular effects**
  - Burning, dryness, irritation, watering

- **Other symptoms**
  - Allergy to plastic
  - Itchiness on the hand
  - Nausea

- **Symptoms reoccur**
  - Upon exposure to new plastics, cleansers, and bleach
# Medical records – Employee #1

<table>
<thead>
<tr>
<th>Day</th>
<th>Subjective complaints</th>
<th>Objective Findings</th>
<th>Diagnosis/Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No medical visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>Sore throat; Cough; Labored breathing; Distorted vision</td>
<td>Exam unremarkable except mild inflamed nasal mucosa and some mild cobble-stoning in the oropharynx</td>
<td>Dx: allergic reaction</td>
</tr>
<tr>
<td>80</td>
<td>Chest tightness</td>
<td>Pulse oximeter room air 98%; Chest x-ray: no significant infiltrate or masses in the lung fields</td>
<td>Dx: Chemical substance; Exposure to fumes, gases and vapor</td>
</tr>
<tr>
<td>86</td>
<td>Chest tightness; Nasal congestion</td>
<td>Unremarkable spirometry</td>
<td>Impression: Irritant-induced reactive airway disease and irritant induced rhinitis.</td>
</tr>
<tr>
<td>142</td>
<td>Sore throat</td>
<td>Exam unremarkable except pharynx mildly injected</td>
<td>Pharyngitis. “…there is a possibility that the gastroesophageal reflux may be playing a part in this…”</td>
</tr>
<tr>
<td>219</td>
<td>Enlarged and tender thyroid; Elevated TSH; Positive TPO antibody</td>
<td></td>
<td>Impression: Subacute thyroiditis; Possible Hashimoto thyroiditis</td>
</tr>
</tbody>
</table>
Medical visits - Employee #1

June 24 - July 31

<table>
<thead>
<tr>
<th>Date</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sep.1</td>
<td>Nose, Throat, Lungs, Ears, EYES, Skin</td>
</tr>
<tr>
<td>Sep.9</td>
<td>Nose, Throat, Lungs, Ears, EYES, Skin</td>
</tr>
<tr>
<td>Sep.16</td>
<td>Nose, Throat, Lungs, Ears, EYES, Skin</td>
</tr>
<tr>
<td>Sep.17</td>
<td>Nose, Throat, Lungs, Ears, EYES, Skin</td>
</tr>
<tr>
<td>Sep.24</td>
<td>Nose, Throat, Lungs, Ears, EYES, Skin</td>
</tr>
</tbody>
</table>

- work period
- doctor visit
- effects: SEVERE, MILD, NONE
# Medical records – Employee #2

<table>
<thead>
<tr>
<th>Day</th>
<th>Subjective complaints</th>
<th>Objective Findings</th>
<th>Diagnosis/Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No medical visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>Shortness of breath; Burning of eyes and nasal mucosa; Headache</td>
<td>Exam unremarkable</td>
<td>No dx made. Patient wants to go home and rest</td>
</tr>
<tr>
<td>59</td>
<td>Breathing difficulty; Burning of eyes</td>
<td>Exam unremarkable</td>
<td>Dx: Probable irritation of eyes and throat, secondary to exposure to fumes</td>
</tr>
<tr>
<td>80</td>
<td>Cough; Voice change; Eye irritation; Heaviness in chest</td>
<td>Exam unremarkable</td>
<td>Dx: Exposure to phosphate ester plasticizers compound; Upper airway irritation</td>
</tr>
<tr>
<td>86</td>
<td></td>
<td>Exam and PFT unremarkable</td>
<td>Impression: Irritant-induced reactive airway disease</td>
</tr>
</tbody>
</table>
Medical visits - Employee #2

July

August

September

Jul.24-
Aug.8

Aug.20
NOSE
LUNGS
EYES
SKIN

Aug.24
LUNGS
EYES
SKIN

Sep.10
THROAT
LUNGS
EYES
SKIN

Sep.16
LUNGS
EYES
SKIN

Sep.16

work period

doctor visit

effects:

SEVERE
MILD
NONE
Specific causation evaluation (toxicology)

- **Was chemical present?**
- **Can chemical cause the effect (at any dose)?**
- **Was exposure sufficiently large and long to cause the effect?**
- **Did effects occur within an appropriate time frame of exposure?**
- **What are alternative causes of the effect?**
Was the chemical present?

- When retained:
  - Cable composition known; coated with
    - Phenol
    - Doverphos 8
      - Triphenyl phosphite
      - Phosphorous acid, diisodecyl phenyl ester
      - Phosphorous acid, isodecyl diphenyl ester
  - Emission characteristics unknown
Was the chemical present?

- Testing (GC/MS)
  - Doverphos 8: No  
    *(constituents not detected)*
  - Phenol: Yes  
    *(detected)*
Is the chemical capable of producing claimed health effects?

<table>
<thead>
<tr>
<th>DOVERPHOS 8 CONSTITUENTS</th>
<th>PHENOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>No toxicological and epidemiological studies showed inhalation exposure to the coating in an occupational environment can cause the claimed health effects.</td>
<td>Irritant effects to mucous membranes noted in animal studies.</td>
</tr>
</tbody>
</table>

Health claims consisted of symptoms but no significant signs.
Was exposure sufficient to cause claimed health effects?

- Doverphos 8 constituents
  - Not detected in emissions testing of cable
  - No scientific literature reported coating material exposures at toxic doses to animals or humans
  - All chemical constituents of coating material were minimally toxic and unlikely to cause any long-term effects
  - Evaporation rate close to that of corn oil (i.e., very slow)

<table>
<thead>
<tr>
<th></th>
<th>Doverphos 8</th>
<th>Corn Oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vapor Pressure (mmHg)</td>
<td>&lt;0.75</td>
<td>&lt;1.0</td>
</tr>
</tbody>
</table>
Was exposure sufficient to cause claimed health effects?

- Phenol

- GC/MS analysis measured emission rate from cable

<table>
<thead>
<tr>
<th>Estimated phenol concentration in room containing 1000 linear feet of cable (with no ventilation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>After 8 hour of emission</td>
</tr>
<tr>
<td>After 2 weeks of emission</td>
</tr>
</tbody>
</table>

OSHA 8-hr PEL | 19 mg/m³ |
Did effects occur within an appropriate time frame?

- Onset of symptoms not documented or reported to have occurred within 24 hours after onset of exposure
- Symptoms were reported to get progressively worse over time
Alternative explanations

- Documented presence of preexisting and/or unrelated medical disorders
  - Hashimoto’s thyroiditis
  - Fuch’s dystrophy
Remember

Differential Diagnosis

Differential Etiology
School Smell

Case #3:

Construction defect
Case #3: School Smell

Gulp! Regence rate boost averages 19 percent for individual plans

For some moving into older age group, increase will total 40 percent

Wing of new Seattle school is closed over strong odor; kids show symptoms

Grieving Fort Lewis’ next worry: a summer even more dangerous
Exposure

- Students and staff complain of “strong odor” of unknown source

- Odor complaints occurred
  - when HVAC was not running on 100% fresh air, 24 hr/day, or
  - when HVAC shut down for maintenance

- Complaints became more frequent with time
Health claims

- Staff and students complained of
  - red, itchy eyes
  - rashes on face, arms
  - sore throat
  - difficulty breathing
  - headache
  - fatigue
  - reproductive problems
A noticeable, irritating odor was present

Industrial hygienists

- Confirmed odor was strongest at concrete/carpet interface
- Collected samples
  - Comfort parameters: all within normal ranges
  - EPA TO-17: no remarkable measurements
Materials scientists

- Collected carpet samples to confirm source of emissions
- Identified carpet interactions with damp, alkaline concrete

Literature searches

- PubMed: no reported effects
- Material science publications: cases of nasal and ocular effects in building occupants to methyl-hexanols
What was the chemical in question?

Wet & alkaline concrete can react with applied adhesive to release VOCs

Emission of 5-methyl-1-hexanol measured in a chamber test

5-methyl-1-hexanol (ng) *

<table>
<thead>
<tr>
<th>Material</th>
<th>Amount (ng)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpet</td>
<td>13,000</td>
</tr>
<tr>
<td>Mastic (Adhesive)</td>
<td>2,000</td>
</tr>
<tr>
<td>Concrete (Fresh)</td>
<td>2,000</td>
</tr>
<tr>
<td>Concrete (Bakeout 48h @ 80F)</td>
<td>500</td>
</tr>
<tr>
<td>Concrete (Bakeout 7d @ 80F)</td>
<td>500</td>
</tr>
</tbody>
</table>

*Amount collected in 6L of nitrogen (0.2L/min flow rate)
Solution to the construction defect

- Removed carpet
- Bead blasted concrete
- Applied correct concrete sealant
- Installed new carpet
End of story

- Hexanols (µg/m³)

<table>
<thead>
<tr>
<th>Time</th>
<th>Room 299</th>
<th>Room 148</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS FOUND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFTER SEALING</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEW CARPET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 DAYS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 DAYS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 WEEKS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 MONTHS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Remember

- Sometimes complex medical complaints require help outside of the biomedical community
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