New and emerging risks and work-related diseases

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Occupational health risk-disease?
Deduction

PAH/UV cause cancer

Roofers exposed to PAH/UV

Roofers have cancer risk
• Hazard identification
  • IARC assessed 900 agents
  • 1000s agents unknown hazards

• Exposure assessment
  • 1 in 5 EU-workers exposed to carcinogens
  • Underestimate?

• Risk assessment
  • ‘Acceptable’ cancer risk: $10^{-5}$
  • Uncertainty

Occupational hazard, exposure and risk
Occupational diseases?
8% EU occupational cancers
Causes and risk
Induction

Individuals with neurological disorders

Diisocyanate probable cause?

Exposure to Diisocyanate
Pharmaco-vigilance

Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem
OSH-vigilance

Science and activities relating to the **detection, assessment, understanding and prevention of adverse effects** or any other **occupational**-related problem
<table>
<thead>
<tr>
<th>Product</th>
<th>Since</th>
<th>Industrial use</th>
<th>First reports on cancer</th>
<th>Important publications/reports</th>
<th>Regulatory steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>1900</td>
<td>Solvent in production of artificial leather, rubber goods, glue, printing, paint, coatings, dry cleaning, automobile manufacturing, etc.</td>
<td>In 1928 first case of benzene-induced leukemia: acute lymphatic leukemia in a pharmaceutical worker with high benzene exposure levels</td>
<td>1977 - Infante et al. publish the first cohort study of workers linking benzene exposure directly to leukemia</td>
<td>1982 -IARC evaluated benzene as having “sufficient evidence that benzene is carcinogenic to man,”</td>
</tr>
<tr>
<td>Radium</td>
<td>1898</td>
<td>Among others, painting watches with radium containing paint</td>
<td>1923 - first bone sarcoma recorded in this group of women in; there have been 55 cancers in a population of nearly 3000 women (incl leukaemia and breast cancer).</td>
<td>1949 - International Committee on Radiological Protection (ICRP): no dose threshold for radiation-induced cancer</td>
<td>1996 - EU Directive on Ionising Radiations based on ICRP 60 which will be mandatory on member states.</td>
</tr>
<tr>
<td>Substance</td>
<td>Worker population/tasks</td>
<td>Observed health effect</td>
<td>Emerging risk (concern)</td>
<td></td>
<td></td>
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<tr>
<td>---------------------------------</td>
<td>--------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
<td>------------------------------------------------------</td>
<td></td>
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<tr>
<td>Formaldehyde</td>
<td>Hair dressers - use of hair straightening products</td>
<td>Irritation skin, eyes and respiratory tract, allergies</td>
<td>Increased/illegal use of the products</td>
<td></td>
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</tr>
<tr>
<td>Indium tin oxide</td>
<td>Manufacture of flat-panel displays (LCD, plasma screen)</td>
<td>Pulmonary fibrosis</td>
<td>New technology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystalline silica (sand)</td>
<td>Sandblasting of textiles</td>
<td>Silicosis</td>
<td>New use, intensified exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic polymeric fibres</td>
<td>Textile workers from a nylon flocking plant</td>
<td>Interstitial lung disease (Flock worker's lung)</td>
<td>New risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricresyl phosphate</td>
<td>Cockpit and cabin crew</td>
<td>'Aerotoxic syndrome' (neurological symptoms)</td>
<td>New exposure scenario</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diacetyl-containing flavorings</td>
<td>flavoring production and application</td>
<td>Bronchiolitis obliterans</td>
<td>New risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-Aminosalicylic acid</td>
<td>Drug manufacturing</td>
<td>Occupational asthma</td>
<td>New risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hexamethylene diisocyanate</td>
<td>Paint quality controller</td>
<td>Acute life-threatening extrinsic allergic alveolitis</td>
<td>New risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dermal exposure is New route of exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylene diphenyl diisocyanate</td>
<td>Orthopedic plaster casts workers</td>
<td>Occupational asthma</td>
<td>exposure levels lower than OEL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Detecting emerging risks for workers and follow-up actions, RIVM Rapport 601353004
New WRD

Disease

Exposure  Work
Modernet.org
Early warning systems

• Detect adverse effects of occupational exposure

• Analysis of health effect-work association

• Case reporting

• Signals: early warning signs of adverse effect
Anosmia

- Male 46 year
- Floor replacement and repair: polyurethane, isocyanides, xylene, styrene
- 2012: sudden loss of sense of smell and taste
- NMR
  - 2012: normal
  - 2014: Atrophy R olfactory bulb and L
- No improvement in 3 years

Known or new?

Search strings for the study of putative occupational determinants of disease

Stefano Mattioli,¹ Francesca Zanardi,¹ Alberto Baldasseroni,² Frederieke Schaaafsma,³ Robin MT Cooke,¹ Gianpiero Mancini,⁴ Mauro Fierro,¹ Chiara Santangelo,¹ Andrea Farioli,¹ Serenella Fucksia,¹ Stefania Curti,¹ Francesco S Violante,²¹ and Jos Verbeek⁵

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Nine ‘aspects of an association’ should be considered before deciding that the most likely interpretation is causation.

“In what circumstances can we pass from an observed association to a verdict of causation? Upon what basis should we proceed to do so?”
1. Strength of association

**Criterion**

- Strong associations less likely caused by chance
- No universal agreement ‘strong’ or ‘weak’ association
  - OR or RR > 2.0 ‘moderately strong’
  - OR or RR > 5.0 ‘strong’

**Diisocyanates**

- No randomized trials or longitudinal cohort studies
- No association in most studies weak association in one report
- One reported: PR of 1.7, (95% C.I. 1.1 – 2.7)
2. Consistency

**Criterion**
- Replication of findings
  - in different populations
  - under different circumstances
  - in different times
  - with different study designs

**Diisocyanates**
- Symptoms in case reports were variable
  - Memory (n=6)
  - Headaches (n=8)
  - Irritability (n=4)
  - Depression (n=6)
  - Paraesthesia (n=4)
  - Anosmia (n=1)
3. Specificity

**Criterion**
- Specific exposure associated with one disease
- Effect has one cause, not multiple causes
- CAVE
  - Many exposures are linked to multiple diseases
  - Many diseases have multiple causes

**Diisocyanates**
None of symptoms or findings is specific
- Anxiety: common in respiratory distressed patients
- Memory loss and depression: associated with a wide variety of causes
4. Temporality

**Criterion**

- Exposure precedes disease
  - Latency and incubation period
- Levels of evidence
  - Randomized control trial (strong)
  - Cohort studies (moderate)
  - Case-control studies (moderate)
  - Cross-sectional studies (weak)

**Diisocyanates**

- Onset of symptoms preceded exposure to diisocyanates
- Cave: baseline comparison and exposure data are lacking in most cases
5. Biologic gradient

**Criterion**
- Dose-response or exposure-response curve with an expected shape
- Changes in exposure are related to trend in risk of disease

**Diisocyanates**
- There is no clear dose response demonstrated
- Biological gradient remains undefined but potentially exists.
6. Plausibility

**Criterion**
- Proposed mechanism should be biologically plausible
- Reference to a “coherent” body of knowledge

**Diisocyanates**
- No mechanisms of toxicity described or proposed
- Biological plausibility remains undefined
7. Coherence

**Criterion**

- Cause-effect interpretation for an association does not conflict with
  - Natural history
  - Biology of disease

**Diisocyanates**

- No early objective effects or other abnormalities
- No specific physiological or biological testing specific to diisocyanates
- Mostly subjective effects
8. Experiment

**Criterion**
- Cessation of exposure
- Cave
  - If the pathogenic process has started, removal of cause does not reduce disease risk
  - Reduction in disease frequency might not be for etiologic reason hypothesized

**Diisocyanates**
- Reversible?
- Animal studies have not demonstrated neurotoxicity from diisocyanate exposure
9. Analogy

Criterion
• Similar exposures can cause similar effects

Diisocyanates
• Diisocyanates are a group of low-molecular weight aromatic and aliphatic compounds
• No reports of similar compounds or agents that result in neurotoxicity
Conclusion

<table>
<thead>
<tr>
<th>Hill's Criterion</th>
<th>Evidence Summary</th>
<th>Probability (%) of criterion being true</th>
<th>Product of discriminant function and probability, ((C1))</th>
<th>Product of discriminant function and probability, ((C2A))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Strength</td>
<td>One study (Nijem) presented relative risk ratio of (1.7*)</td>
<td>60</td>
<td>(-14.7799)</td>
<td>(-10.0835)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(3.7338 (0.06223 \times 60))</td>
<td>(1.1538 (0.01923 \times 60))</td>
</tr>
<tr>
<td>2. Consistency</td>
<td>Studies varied in symptoms and findings**</td>
<td>50</td>
<td>(2.0305 (0.04061 \times 50))</td>
<td>(0.9015 (0.01803 \times 50))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Specificity</td>
<td>No findings specific to diisocyanates</td>
<td>40</td>
<td>(-1.1148 (-0.02787 \times 0))</td>
<td>(-1.5508 (-0.03877 \times 0))</td>
</tr>
<tr>
<td>4. Temporality</td>
<td>All case reports preceded by diisocyanates exposure</td>
<td>100</td>
<td>(7.657 (0.07657 \times 100))</td>
<td>(8.281 (0.08281 \times 100))</td>
</tr>
<tr>
<td>5. Biologic gradient</td>
<td>Dose-response data lacking**</td>
<td>50</td>
<td>(-1.764 (-0.03528 \times 50))</td>
<td>(-1.767 (-0.03534 \times 50))</td>
</tr>
<tr>
<td>6. Plausibility</td>
<td>No mechanism of toxicity found</td>
<td>0</td>
<td>(0.00 (0.23025 \times 0))</td>
<td>(0.00 (0.21689 \times 0))</td>
</tr>
<tr>
<td>7. Coherence</td>
<td>No early objective effects or other abnormalities were measured as a result of exposures</td>
<td>0</td>
<td>(0.00 (0.009621 \times 0))</td>
<td>(0.00 (0.00334 \times 0))</td>
</tr>
<tr>
<td>8. Experimental evidence</td>
<td>Animal studies have not demonstrated neurotoxicity from diisocyanate exposure</td>
<td>0</td>
<td>(0.00 (0.00843 \times 0))</td>
<td>(0.00 (0.00659 \times 0))</td>
</tr>
<tr>
<td>9. Analogy</td>
<td>Data to similar class of agents lacking**</td>
<td>50</td>
<td>(-0.6470 (-0.01294 \times 50))</td>
<td>(-0.5055 (-0.01011 \times 50))</td>
</tr>
<tr>
<td>Sum</td>
<td></td>
<td>Sum</td>
<td>(C1 = -4.8844)</td>
<td>(C2A = -3.5705)</td>
</tr>
</tbody>
</table>

\[
e^{C1} / (e^{C1} + e^{C2A}) = 21.2\%
\]

Conclusion

Journal of Clinical Epidemiology

Original Article

A weight of evidence approach to causal inference

Gerard Swaen\textsuperscript{a}, \textsuperscript{a}, Ludovic van Amelsvoort\textsuperscript{b}

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http://dx.doi.org.kuleuven.ezproxy.kuleuven.be/10.1016
/j.jclinepi.2008.06.013

Abstract
Conclusion

• Diisocyanates: not sufficient evidence

• Solvents: influence on senses (reversible)

• Parkinson or Alzheimer disease?
**Conclusion**

*BMJ Case Reports* 2015; doi:10.1136/bcr-2015-212936

**CASE REPORT**

**Ear and vestibular symptoms in train operators after sudden air pressure changes in trains**

Hugues M A Francois¹, Luc Vantrappen¹, Vincent Van Rompaey², Lode Godderis³

Accepted 4 December 2015
Published 17 December 2015

**Summary**

A healthy 31-year-old train operator presented to our occupational health clinic reporting ear aches, headaches, dizziness, unsteadiness and even slight tinnitus. These symptoms first appeared when the patient started operating from a new train cabin. He described a sudden pressure gradient, experienced on some parts of the trajectory, which might have caused these problems. Although the cabinets were equipped with a pressure equalising device, this was usually switched off because of the device creating an uncomfortable feeling in the cabin. The literature describes sudden pressure gradients as possible factors for passenger discomfort.

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**Ruik je dat niet? Reukstoornissen door blootstelling in het werk**

Annet Lenderink, Sanne Maleska, Lode Godderis

Beroepsziekten
First Online: 15 April 2016
DOI: 10.1007/s12498-016-0072-2

Samenvatting

Veel mensen ervaren wel eens dat ze minder goed kunnen ruiken, bijvoorbeeld na een verkoudheid. In zo'n periode is ook de smaak minder, maar gelukkig herstellen reuk en smaak zich meestal vanzelf weer, nadat de verkoudheid is verdwenen. Toch kan het reukvermogen door uiteenlopende oorzaken ook langdurig of blijvend worden aangetast en dat heeft grote invloed op het welbevinden en het functioneren van mensen.
Overall caveats to “criteria”

“None of my ... [criteria] can bring undisputable evidence for or against the cause-and-effect hypothesis and none can be required as a sine qua non.”

Sir Austin Bradford Hill (1965)
Other algorithms

A study of agreement between the Naranjo algorithm and WHO-UMC criteria for causality assessment of adverse drug reactions

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This is an open-access article distributed under the terms of the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Should we abandon the periodic health examination?

**YES**

In 2009, KIS Health published a statistical snapshot of the top 10 cancer survivors in Canada while family physicians and other specialists. Second only to visits for hypertension was "general medical care" at $133 million per year. Assuming three-day service utilization, and considering that on average a routine medical examination also known as an annual physical or a periodic health examination (PHE) takes up about a day of a regular appointment, this represents approximately 210 million appointments a year at an expense of $2 billion in construction costs alone. Add to this the expense of all the unnecessary testing, investigations, and in fact, I would estimate the total cost to be much greater.

**Outdated**

Historically, the annual physical is a grounded head-to-toe examination, accompanied by comprehensive multisectional investigation and laboratory screening. The roots of the annual physical date back to 1881 with ophthalmology being the prime examining role for its continuous, and individual, nature. Even while the Canadian Task Force on the Periodic Health Examination and the United States Preventive Services Task Force recommended abandoning the comprehensive systematic examination in favour of case-finding maneuvers during regular visits, schools, and other appropriate evidence-based procedures, the periodic health examination remains a valuable cornerstone and possible comprehensive health assessment, which claims to be evidence-based. These assessments cannot take anywhere from a few to a dozen studies. These investigations, such as whole-body computed tomography scanning, and might in fact be more harmful than beneficial.

**Better use of resources**

Of particular importance is that patients who already regularly visit family physicians, and even patients who already have 4 or more chronic disease visits per year, are less likely to schedule dedicated PHEs. There is no convincing evidence that having a dedicated appointment for a PHE in place of case-finding maneuvers during regular visits leads to better health outcomes, or that those who undergo this annual exam are healthier or have decreased morbidity and mortality compared with those who do not. In fact, there is insufficient evidence to show that any of the investigations conducted during the PHE might be harmful and not in the best interest of the patient. Advocating for patients has included not subjecting them to unnecessary medical interventions, and both the CMA Code of Ethics and the College of Family Physicians of Canada’s Code of Family Medicine take on a responsibility for the judicious use of health care resources.

A disturbing emerging trend is that of practices offering improved access and services for an annual assessment. One of the cornerstone of the "improved care" offered by these practices is a comprehensive health assessment, which claims to be evidence-based. These assessments can take anywhere from a few to a dozen studies. These investigations, such as whole-body computed tomography scanning, and might in fact be more harmful than beneficial.

Time for prevention

Many provincial health care systems in Canada consist of a fee-for-service health examination, a visit usually double the time of the average visit. By necessity, this is not only time for physicians to do their best, but also time for patients to be examined and their problems addressed.

**NO**

It is often difficult to dedicate time for preventive care. A busy family practice. Patients rarely turn to their family doctor more for specific health complaints than for routine preventative care. The periodic health examination (PHE) is a tradition in North America, but it is not used in most other countries, such as the United Kingdom, where preventive care is still delivered. Do we really need the PHE in Canada?

The PHE can advance critical elements of care for our patients’ relationship building and preventive care. A large systematic review of studies on the value of periodic health examination found that the PHE was found to be associated with an improved delivery of health-related health education, care coordination, and overall health outcomes.

The PHE was also found to decrease patient worry. A third of the studies reviewed were done before 1990, before larger scale dissemination of Canadian and American task force recommendations on preventive care. As the number of evidence-based preventive care recommendations grows, a PHE that often planned focus on preventive care might become even more valuable.

**Outdated**

Preventive care is becoming more important than ever, especially in the absence of routine preventive care. Preventive screening is a cornerstone of preventive care, and without it, we miss the chance to detect and prevent disease.

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Guidelines for Occupational Medical Examinations

PROPHYLAXIS IN OCCUPATIONAL MEDICINE

Gentner Verlag
Conclusion

• Easy access to OSH for all
• Regular contact
• Periodicity depends on age, work, objective and outcome of surveillance
• Periodicity should not hinder to tackle problems
• Surveillance is an important means in preventing Work related diseases
“Scientists believe in proof without certainty; most people believe in certainty without proof.”