Chemical Contamination

Risk Prevention in Infusion Therapy

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Chemical Contamination

Definition
The term chemical contamination is defined as the unintended exposure of a healthcare professional to hazardous drugs.

The American National Institute for Occupational Safety and Health (NIOSH) defines a hazardous drug as any drug identified by at least one of the following criteria: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, or new drugs that mimic existing hazardous drugs in structure or toxicity [NIOSH 2004]. 136 hazardous drugs are listed, including:
- Chemotherapy/cytotoxic agents
- Antibiotics/Antivirals
- Bioengineered drugs
- Monoclonal antibodies
- Gene & hormone agents
- Other miscellaneous drugs

Causes
This brochure will give an outline on the causes of chemical contamination.

Kromhout and others have noted that the exact cause or pathway of this exposure is unclear [Kromhout et al. 2000], but two primary routes can be found in the literature: a dermal [Valanis et al. 1993a, b] and an aerosol route [Kromhout et al. 2000].

Dermal contamination
There are many areas where contamination has been found and which have been identified as leading to dermal, or ‘touch’, contamination. These include:
- the surface of vials [Mason et al. 2003],
- the surface of drug boxes [Schmaus et al. 2002],
- preparation of drugs such as cyclophosphamide [Fransman et al. 2004]
- and handling bodily fluids of patients undergoing cytostatic treatment [Fransman et al. 2004, Kromhout et al. 2000].

The presence of contamination in these areas suggests that preparing cytostatics as well as handling vials, boxes and bodily fluids is a cause of contamination.

Other causes of contamination, discussed by regulatory bodies such as the NIOSH, are poorly decontaminated spills, the priming of IV sets, handling outside of the pharmacy and poor product choice [NIOSH 2004].

Fig. 1: Contamination caused by priming of IV sets
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**Fig. 2: Contamination caused during preparation**

"The results show that pharmacy technicians and oncology nurses were dermally exposed to cyclophosphamide". [Fransman et al. 2004]

**Aerosol contamination**

Aerosol contamination during preparation and delivery is accepted by bodies such as NIOSH and can be found in the literature [Neal et al. 1983, NIOSH 2004, Sessink 1994]. Certain studies, however find no evidence for aerosol contamination but it has been suggested that this is due to inadequate detection limits [Larson et al. 2003].

**Risks**

**Skin contact during:**
- Contact with vial surfaces
- Contact with packaging surfaces
- Handling bodily fluids of patients
- Spills
- Priming IV sets

**Aerosol contact during:**
- Preparation of drugs
- Administration of drugs
The consequences of chemical contamination depend on the drug in question. For this reason, a differentiation between toxic and non-toxic contamination seems appropriate.

**Non-toxic contamination**
Exposure to non-toxic medications such as certain antibiotics is not without consequences and has been shown to lead to dermatitis [Gielen and Goossens 2001] and hypersensitivity [AFS 2005] which can reduce working efficiency.

**Toxic contamination**
1. **Acute symptoms**
Drug SPCs are the principle source of information regarding undesirable effects and should be consulted regularly. Paclitaxel, for example, is said to lead to acute symptoms such as nausea, alopecia (hair loss) and bradycardia [Paclitaxel SmPC 2010]. Studies show a significant increase in similar acute symptoms between control cases and cases exposed to antineoplastic agents (e.g. diarrhea, throat irritation, skin rashes) [McDiarmid et al. 1988, Valanis et al. 1993a]. However, the main acute symptom is mutagenicity. Studies have found various mutagenicity indicators such as sister chromatid exchange or aberrations [Falck et al. 1979, Sarto et al. 1990]. Since chromosomal mutagenicity following exposure is stochastic in nature [Health Counsel 1994], as little as one molecule could cause a mutation. For this reason, regulatory bodies do not quote threshold levels under which exposure is acceptable.

2. **Chronic symptoms**
   **Carcinogenicity**
Mutagenicity, while being an acute symptom in itself, can lead to the chronic disease cancer. The link between exposure to high dose cytotoxic medication and secondary malignant neoplasia has also been shown, and has led to the International Agency for Research on Cancer (IARC) classifying many antineoplastic drugs as group 1 (carcinogenic to humans) compounds [IARC]. The stochastic nature of carcinogenicity makes even low doses, such as those found during a contamination, a risk. Studies showing such a link are subject to certain statistical challenges due to the low occurrence of cancer in the population and limited sample sizes. However, Sessink calculated that the theoretical lifetime risk that a healthcare worker suffers from leukemia was 95-475 per million [Sessink et al. 1995]. Skov shows an increased risk of leukemia and non-Hodgkin’s lymphoma in hospital workers [Skov et al. 1992].

   **Reproductive effects**

   **Other chronic effects**
As further possible consequences, Sotaniemi showed chronic liver damage and fibrosis [Sotaniemi et al. 1983] as a result of exposure to toxic drugs.

"The results showed that nurses exposed to antineoplastic agents at work were significantly more likely to have urinary mutagenicity, as compared to nonexposed nurses ... A significantly higher proportion of untoward pregnancy outcomes occurred in pregnancies with exposure to antineoplastic agents." [Rogers and Emmett 1987]

"A statistically significant association was observed between fetal loss and occupational exposure to antineoplastic drugs during the first trimester of pregnancy." [Selevan et al. 1985]
Fig. 3: Causes of chemical contamination and their potential consequences.
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Consequences

The costs factors here will be split into the cost to society and the cost to the healthcare institutions which will be discussed below (see Fig. 4).

**Cost for the hospital**

Common standard operating procedures (SOPs) in hospitals as well as published guidelines dictate that healthcare workers exposed to contamination must thoroughly rinse the exposed area with water for ten minutes. If the eyes are contaminated, an ophthalmologist is to be consulted [QuapoS 2003]. Added to this lost productivity, there are some hardware costs for washes, ointments, bandages and medication to ease the symptoms of any acute consequences such as diarrhea.

The dermatitis and hypersensitivity caused by repeated exposure to medication has not been investigated with regard to cost, but Mäkkinen found that healthcare workers with an occupational skin disease had to take sick leave (21%) or were forced to change occupation (21%) [Mäkkinen 2009]. The reduction of the working efficiency of staff who stay, and the training of new staff to replace those who leave, are two cost factors that must not be forgotten.

Another case where a complication leads to loss of productivity is cancer; for example, in the UK, patients are allocated up to 28 weeks statutory sick leave with a sick pay of 79.15 € (90 €) per day [Macmillan cancer support 2010].

In a similar way, hospital costs associated with the reproductive complications such as fetal loss, are caused when compassionate sick leave is granted to the healthcare worker. While this will certainly vary significantly, the legal minimum leave for the loss of a 1st degree relative for many industries in Germany is 2 days [IGBCE 2000].

Depending on the country one can imagine, that if any of these health problems can be traced back to poor safety procedures, there may be costly legal consequences for a healthcare institution.
### Examples of complications resulting from Chemical Contamination

<table>
<thead>
<tr>
<th>Severity</th>
<th>Treatment</th>
<th>Cost to healthcare system/ Insurance companies</th>
<th>Source of direct cost to Hospital</th>
<th>Cost to Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Medication &amp; radiotherapy, Surgery, Diagnostic procedures, Consultations, Psychological care, Psychological care for parents, Possible surgery for child, Prosthetics</td>
<td>12,950 €</td>
<td>28 weeks sick leave, sick pay</td>
<td>26,600 €</td>
</tr>
<tr>
<td>Medium High</td>
<td>If in later pregnancy weeks: Surgery, Psychological care for parents</td>
<td>20,520 €</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Medium</td>
<td>Medication, Specialist consultation</td>
<td>---</td>
<td>Sick leave, retraining</td>
<td>---</td>
</tr>
<tr>
<td>Low</td>
<td>Consultations, No complication</td>
<td>---</td>
<td>Disinfectant, cream, plaster emergency, eye wash kit, gloves, test time for consultation</td>
<td>---</td>
</tr>
</tbody>
</table>

Fig. 4: Estimation of possible additional costs as a consequence of complications caused by chemical contamination.
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Fig. 5: Centralized pharmacy preparation

Fig. 6: Safety devices

Fig. 7: Protective coverings in use in a laminar air flow cabinet
Preventive strategies
Preventative strategies are often recommended by national bodies (see box) and focus on reducing exposure. The pictures (left) illustrate the main precautions, namely:

- Prevent contamination caused by handling errors by centralizing preparation [QuapoS 2003]. This allows medication to be handled by specially trained personnel (Fig. 5).
- Prevent release of toxic contamination by using "safety" devices [NIOSH 2004]. These aim to reduce aerosol contamination (e.g. aerosol filters) as well as drip contamination (e.g. needle free devices) (Fig. 6).

Some causes of contamination such as the vial surface, however, are difficult to prevent and so must be contained (Fig. 7):

- Any aerosol contamination which is formed is contained by using laminar air flow (LAF) or isolator cabinets [Nguyen et al. 1982, Crauste-Manciet et al. 2005].
- Any drip contamination which is formed is prevented from being absorbed by use of protective coverings such as gowns, masks and gloves [ASTM 2005].

In addition, regular controls such as blood tests are recommended in order to monitor exposure levels [QuapoS 2003]. If systematic protective measures are put in place, exposure can be reduced [Ündeger et al. 1999, Skov et al. 1992].

Regulatory bodies
The following bodies (among others) publish recommendations for the prevention of chemical contamination:

- The National Institute for Occupational Safety and Health (NIOSH), USA
- Centers for Disease Control and Prevention (CDC), USA
- International Society of Pharmacovigilance (ISOP)
- German Society for Oncology Pharmacy (DGOP), Germany
- Swedish Work Environment Authority (AFS), Sweden
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**Risk prevention**

**Mini-Spike® Chemo V**  
Vented dispensing pin for safe and convenient fluid transfer with syringes.  
- Air vent includes inbuilt filter to prevent toxic aerosols from escaping.  
- Two-way valve prevents drips and spills.

**Cyto-Set® Mix**  
The complete system solution for safe and easy toxic preparations  
- Allows needle free admixture into infusion container.  
- Optimal system compatibility with Cytoset.

**Ecoflac® plus**  
The state of the art IV solution container that offers safe and convenient application of all IV procedures from drug admixture to drug delivery.  
- Superior properties of the resealable port membrane prevent drips.  
- Innovative cap design allows a safe and easy drug admixture process and secure spiking.

**Safeflow / Ultrasite®**  
Valves for safe and convenient access to the infusion line. The valve ensures the system remains closed.  
- B. Braun's needle-free infusion systems reduce the risk of drip contamination and reduce use of needles.
Ecoflæ® Connect
Closed system transfer cap for single dose drug admixture.
- The closed system of Ecoflæ® Connect ensures that there is no contact with the external environment.
- This closed system reduces exposure of healthcare professional to the medication.

Intrafix® SafeSet
IV set for safe and convenient infusions.
- Automated, drip free priming through innovative Prime Stop membrane built into the end cap.

Cyto-Set®
The complete system solution for safe and easy toxic infusions.
- Toxic drips prevented by allowing simple pre- and post-filling of the line with neutral solution.
- Design prevents need for re-spiking.

Discofix® C
The unique stopcock for premium safety.
- A special material prevents toxic drips out of system by eliminating stress cracks.
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Literature


ASTM. D6978-05: Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs, American Society for Testing and Materials 2005


Hemminki K, Kyyrön M, Lindbohm M–L. Spontaneous abortions and malformation in the offspring of nurses exposed to anaesthetic gases, cytostatic drugs, and other potential hazards in hospitals, based on registered information of outcome. J Epidemiol Community Health 1985; 39: 141–147


IGBCE. Manteltarifvertrag 2000


Nguyen TV, Theiss JC, Matney TS. Exposure of pharmacy personnel to mutagenic antineoplastic drugs. *Cancer Res* 1982; 42: 4792–4796


Paclitaxel SmPC. BMS 2010

QuapoS 3 Quality Standard for the Oncology Pharmacy Service with Commentary. Institute for Applied Healthcare Sciences (IFAHS e.V.) for the German Society of Oncology Pharmacy (DGOP e.V.). 2003


The summarized scientific information in this document has been prepared for healthcare professionals. It is based on an analysis of public literature and guidelines. The intention is to give an introduction to the risks commonly associated with infusion therapy and to increase the awareness of healthcare workers to these kinds of problems. Due to its summary nature, this text is limited to an overview and does not take into account all types of local conditions. B. Braun does not assume responsibility for any consequences that may result from therapeutical interventions based on this overview.