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HAZARDOUS DRUG SAFE HANDLING: WHERE ARE WE?

Objectives

- Describe the evidence for adverse outcomes from occupational hazardous drug (HD) exposure
- State current recommendations for minimizing hazardous drug exposure
- Discuss the need for future research related to occupational hazardous drug exposure

Defining Terms:

- High Risk/ High Alert drugs (patients)
  - Drugs requiring special attention due to higher risk of side effects
  - Drugs with narrow range of therapeutic efficacy
  - Drugs that are more difficult to administer
- Hazardous drugs (workers)
  - Drugs requiring careful handling to prevent occupational exposure

Criteria for Hazardous Drugs

- Carcinogens
- Genotoxins
- Teratogens
- Reproductive toxins
- Organ toxicity at low doses
- Structure or toxicity similar to drugs classified as hazardous

(ASHP, 2006; NIOSH, 2004)

Known Human Carcinogens (IARC Group 1)

- Arsenic trioxide
- Azothiaprine
- Busulfan
- Chlorambucil
- Cyclophosphamide
- Etoposide
- Melphalan
- Semustine
- Tamoxifen
- Thiotepa
- Treosulfan
- MOPP*
- ECB*

International Agency for Research on Cancer (IARC)
http://www.iarc.fr/

IARC Groups 2A / 2B

Probable Carcinogens

- **Azacitidine**
- **Carmustine**
- **Cisplatin**
- **Doxorubicin**
- **Lomustine**
- **Nitrogen mustard**
- **Procarbazine**
- **Teniposide**

Possible Carcinogens

- **Amsacrine**
- **Bleomycin**
- **Dacarbazine**
- **Daunorubicin**
- **Mitomycin**
- **Mitoxantrone**
- **Streptozocin**

http://www.iarc.fr/

Evidence for Adverse Outcomes: Occupational Hazardous Drug Exposure

Concept of Risk

- What is the association between exposure & development of disease?
- If an association exists, how strong is it?

Measuring Risk

Relative risk = incidence in exposed / incidence in non-exposed

RR = 1 No difference

RR > 1 Risk in exposed is greater

Odds Ratio: = Odds that a case was exposed / Odds that a control was exposed

OR = 1 No difference

OR > 1 Exposure is positively related to disease

Gordis, 2004

Genotoxic Adverse Outcomes

- Genotoxicity in exposed nurses
  - 50% increase in DNA single strand breaks
  - Significantly greater DNA tail length (Comet Assay)
- Chromosomal abnormalities in exposed nurses
  - Significant increase in structural chromosome abnormalities

Yoshida et al, 2006; Testa et al, 2007

Chromosome Abnormalities: Alkylating Agent Handling

Location of Chromosome Abnormality	100 Event IRR*	200 Event IRR*	*p* value
Chromosome 5	2.92	8.54	**0.01**
Chromosome 7	2.31	5.33	0.11
Chromosome 5 or 7	2.62	6.86	**0.001**
Chromosome 11	1.17	1.37	0.79

**IRR= Incidence Rate Ratio: Association between chromosome abnormality rates at select drug handling frequencies compared to zero drug handling events (controls).*

McDiarmid, 2010

Cancer Occurrence

- Increased occurrence of cancer in pharmacy technicians (RR = 1.1-3.6)
- Increase in acute leukemia in exposed nurses (RR = 10.65)
- Overall increased occurrence of cancer in exposed nurses (OR = 3.27, *p* = .03)

RR = Relative Risk; OR = Odds Ratio

Hansen & Olsen, 1994; Martin, 2003; Skov et al, 1992)

Adverse Reproductive Outcomes

- Infertility (OR = 1.42-1.5)
- Spontaneous abortion/ miscarriage
  - 2-3.5 fold increased risk
- Premature labor (OR = 2.98)
- Pre-term birth (OR = 5.56)
- Learning disabilities in offspring (OR = 2.56)

(Fransman, 2007; Hansen & Olsen, 1994; Lawson, 2012; Martin, 2005; Skov, 1992)

Nurses Experience of Adverse Health Effects

- ***"In retrospect, it was very obvious to me. The exposure was there and I had this problem. The exposure was gone and I didn't have it and never have had it again."*** *(speaking about her chronic nasal sores.)*
- ***"The next day I would get up with blood in my urine and bladder spasms, and it was only the day after I mixed; and since I've quit mixing like that, I don't have them now."*** *(Referring to cyclophosphamide.)*

Polovich, 2009

Evidence for Occupational Hazardous Drug Exposure

Patients vs. Health Care Workers Exposure

- **Patients**
  - Therapeutic doses
  - Few drugs
  - Over months
- **Health care workers**
  - Low-doses
  - MANY drugs
  - Over several years

Potential Routes of Exposure

- Dermal absorption:
  - Direct drug contact
  - Contact with contaminated surfaces
- Injection:
  - Sharps
  - Breakage
- Ingestion via contaminated:
  - Food, gum
  - Hand-to-mouth transfer
- Inhalation:
  - Aerosols
  - Vapors

ASHP, 2006; NIOSH, 2004; Polovich, et. al. (ONS), 2009; Polovich, 2011

Summary of Published Evidence

- Contamination on external vial surfaces
  (>15 studies since 1992)
- Excretion of drugs and drug metabolites in urine of health care workers
  (>25 studies since 1992)
- Workplace surface contamination
  (>60 studies since 1994)

Surface Contamination: Two U.S. Studies

1999

- 6 hospitals
- 3 drugs
- Pharmacy: 75% wipe samples > LOD
- Nursing: 65% wipe samples > LOD

2010

- 3 hospitals
- 5 drugs
- Pharmacy: 75% wipe samples > LOD
- Nursing: 43% wipe samples > LOD

LOD = Limit of Detection

Connor et al, 1999; Connor et al, 2010.

Oncology Nurses: Exposure

- Reported during routine handling:
  - 11-17% Dermal or eye exposure (previous year)
  - 4-11% Skin contact (previous week)
  - 12-24% Taking home contaminated clothes
  - 1.4% Sharps injury involving chemotherapy (previous year)
- Spills:
  - 12% reported spills (previous week)
  - Multiple staff usually involved in spill clean-up
  - Staff reporting spills had HDs in urine
  - Staff who *DID NOT* report spills had HDs in urine

Boiano, 2014; Boiano, in press; Friese, 2012; 2014

Implications for Practice

- Routine medication handling results in hazardous drug exposure
- Knowing what drugs are *hazardous* is essential
- Safe handling precautions reduce exposure
- Any worker who fails to follow precautions puts themselves and others at risk

Controlling Hazardous Drug Exposure

Hierarchy of Controls

Most Effective

- **Eliminate the hazard**
- **Engineering controls**
- **Administrative controls**
- **Work practice controls**
- **Personal protective equipment**

Least Effective

U.S. Dept. of Labor, 1998

Engineering Controls: Highest Level Protection

- Machines or equipment
  - Biologic Safety Cabinet (BSC) *or*
  - Compounding Aseptic Containment Isolator (CACI)
  - Closed system transfer device (CSTD)
- Advantages:
  - **Contain** the hazard
  - **Independent** of the worker

ASHP, 2006; NIOSH, 2004; ONS,. 2011

Definitions:

- Closed System
  - Device used to transfer a sterile drug from one container to another
  - Goals: *maintain sterility of the product*
- Closed System Transfer Device
  - Device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of liquid or vapor out of the system
  - Goal: *maintain sterility AND prevent escape of drug*

NIOSH, 2004

Administrative Controls

- Written policies & procedures
- Hazardous Drug List
- Education & competency
- Medical Surveillance
- Alternative duty around pregnancy

Organizational Policies

Content	*% Sites*
Required qualifications for HD handling	100%
Required PPE for chemotherapy handling*	100%
Chemotherapy disposal	100%
Transporting chemotherapy	100%
Chemotherapy spill management	100%
Acute exposure management	80%
Health monitoring of personnel	45%

**25% of organizations did not require gowns for HD handling.*

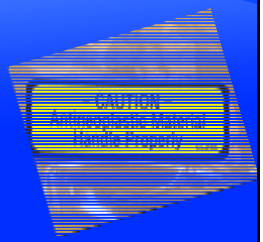
Polovich & Clark, 2012

Education, Training & Monitoring

- Education
  - Classroom instruction (90%)
- Training
  - Supervised practice with preceptor (100%)
  - Skill checklist (60%)
- Monitoring
  - Formal mechanism (25%)
  - Informal "spot checks" (50%)
  - None (25%)

Polovich & Clark, 2012

Work Practice Controls



- Label HDs as hazardous
- Transport HDs in sealed bags
- Inspect HD containers for leaks
- Wash hands after removing PPE
- Avoid touching unnecessary items with contaminated gloves
- Avoid wearing PPE outside drug handling areas
- Avoid spiking & priming (without a closed system)
- Discard used IV equipment intact

Personal Protective Equipment (PPE)

- **Gloves**:
  - *two pair, tested with hazardous drugs*
  - powder-free
  - latex, nitrile, neoprene
- **Gowns**:
  - *tested with hazardous drugs*
  - disposable, single-use
  - cuffs
  - back closure

ASHP, NIOSH, OSHA, ONS

More PPE…

- **Eye protection**
  - when splashing is possible
- **Respirator/mask**
  - aerosols & spills

Double Gloves

- To protect against permeation of some drugs
  - Carmustine
  - Thiotepa
- To prevent transfer of contamination from outer gloves to hands and other surfaces
  - ALWAYS consider gloves contaminated after chemotherapy handling *(5 studies since 1992)*

Use of Hazardous Drug Precautions

Nurses reporting use of HD precautions 'Always' or 76-99%

Precaution	Preparation (n = 32)	Administration (n = 164)	Disposal (n = 154)	Handling Excreta (n = 120)
Chemotherapy gloves	90%	78%	74%	55%
Double gloves	12%	19%	18%	18%
Chemotherapy gowns	64%	56%	53%	30%
Eye protection	25%	17%	12%	17%
Respirator	6%	4%	5%	9%
Overall precaution use:				
Mean score (0-5*)	2.7	2.0	1.9	1.6

*5 = Always; 4 = 76-99%; 3 = 51-75%; 2 = 26-50%; 1 = 1-25%; 0 = Never (Polovich & Clark, 2012)

Predictors of HD Precaution Use

	p value
Fewer barriers	.003
Better workplace safety climate	.006
Fewer patients per day	.027

Polovich & Clark, 2012.
Regression Analysis: R^2 = .06 for Step 1, p = .002; ΔR^2 = .23 for Step 2, p < .001

Practice Environment Impact

	Odds Ratio
Staffing and resource adequacy	**0.35 (0.17-0.73)**
Chemotherapy verified by 2 nurses	**0.17 (0.05-0.59)**
Nurse participation in practice affairs	0.51 (0.24-1.06)
Average workload, last shift	1.06 (0.99-1.12)

* Nurses who reported exposure to chemotherapy in their skin or eye in the past year. Adjusted for individual nurse characteristics (race, certification, education), and clustered observations.

- **Staffing adequacy reduced the odds of exposure by 65%**
- **Chemo verification reduced the odds of exposure by 83%**

Friese, et al., 2010

Barriers to HD Precaution Use

- Things that interfere with HD precaution use
- "Unavailability, inconvenience, expense, difficulty, or time consuming nature of a particular action"
- Examples:
  - Practical (lack of / unacceptable protective equipment)
  - Psychosocial (worker / peer attitudes)
  - Environmental (safety climate)
  - Situational (time constraints)

(Pender, et al., 2006, p. 53)

Top Barriers to Using PPE*

	Agree
PPE makes me feel too hot	61%
PPE is uncomfortable to wear	54%
PPE makes it harder to get the job done	28%
Others around me don't use PPE	33%
People would think I am overly cautious	19%

As barriers increased,
use of precautions decreased

*Polovich & Clark, 2012

Managers' Stated Reasons for Non-Adherence to HD Precautions

- Gowns not provided
- Too busy or rushed
- Gowns uncomfortable
- Lack of concern
- Urgent patient situation
- Lack of knowledge
- Forgetting
- Poor fitting gloves
- Concern for cost
- Patients' objections
- Precautions "too extreme"

Polovich & Clark, 2012

Future Research

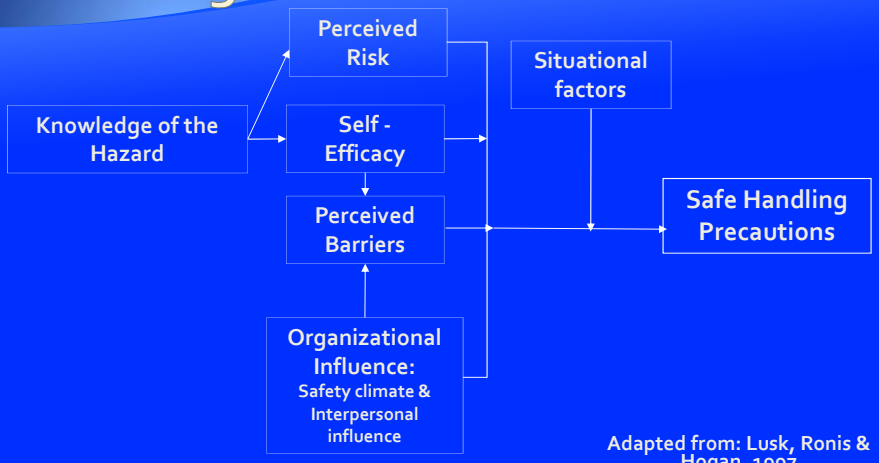
Biological Monitoring for HD Exposure

- HD residue in sweat (treated patients)
- HD exposure following spill clean-up/ acute exposure
- Effective medical surveillance practices

Adverse Health Outcomes of Occupational HD Exposure

- Incidence of adverse health outcomes
- Individual risk factors
  - Cross sectional survey of HD handlers
    - Advantage: ease of data collection
    - Disadvantage: self-reported data
  - Registry for HD handlers
    - Advantages: prospective/ longitudinal data collection linking of work with health outcomes
    - Disadvantages: **$$$,** subject mortality

Factors Predicting Use of HD Safe Handling Precautions



Adapted from: Lusk, Ronis & Hogan, 1997

Overcoming Barriers to HD Precaution Use

- Descriptive:
  - Replicate manager study (large sample)
  - Identify additional barriers
- Experimental:
  - Effects of selected interventions on HD precaution use
  - Effects of selected interventions on HD exposure
  - Impact of practice environment changes

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