

The Hazardous Drug Problem


The Hazardous Drug Problem

How To Ensure Your Safety

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The Hazardous Drug Problem

Most of the information contained in this presentation is based on the ONS Safe Handling of Hazardous Drugs, 2nd Edition.



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The Hazardous Drug Problem

Objectives

- Summarize recent and historical evidence for healthcare worker exposure to hazardous drugs
- Identify work practices that present a risk for hazardous drug exposure
- Outline interventions, including proper use of equipment and devices
- Describe the role of CSTDs in reducing exposure, and practical considerations for selecting a device

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3 Important Questions



What are the dangers?
(and why should I care?)



How am I at risk?



How can I ensure my safety?

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1 What are the dangers?
(and why should I care?)

Because chemotherapy is hazardous

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Still A Necessary Evil

- Most cancer is still treated with chemotherapy, either alone or in combination with other modalities.

Brain Cancer	Lung Cancer
Colon Cancer	Multiple Myeloma
Osteosarcoma	Ewing Sarcoma
Gastric Cancer	Ovarian Cancer
Leukemia	Breast Cancer
Lymphoma	Prostate Cancer
Rhabdomyosarcoma	Melanoma
Testicular Cancer	Myelodysplastic Syndrome
Wilms Tumor	Neuroblastoma

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IV Chemotherapy: 1940-1999

1940s	1950s	1960s	1970s	1980s	1990s
Nitrogen Mustard	Methotrexate	5-FU	Doxorubicin	Carboplatin	Gemcitabine
	Cyclophosphamide	Vincristine	Cisplatin	Etoposide	Vinorelbine
		Cytarabine	Bleomycin	Melphalan	Paclitaxel
				Ifosfamide	Docetaxel
				Dacarbazine	Liposomal Doxorubicin
				Carbustine	Irinotecan
					Arsenic trioxide
					Fludarabine
					Epirubicin
					Topotecan

25 agents in 60 years

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IV Chemotherapy: 2000-2013

2000-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013
Bortezomib	Clofarabine	Temsirolimus	Bendamustine	Eribulin mesylate	Brentuximab vedotin
Oxaliplatin	Azacitidine	Ixabepilone	Romidespin	Cabazitaxel	Vincristine Liposome
	Abraxane		Pralatrexate		Carfilzomib
	Pemetrexed		Nelarabine		Ado-trastuzumab


18 new agents in 14 years

Hazardous drugs are not going away

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What makes hazardous drugs so hazardous?



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Hazardous Drugs Defined

- Any of the following characteristics:
 - Carcinogenicity (cancer in animals or humans)
 - Genotoxicity (genetic mutation)
 - Teratogenicity (fetal defects)
 - Reproductive toxicity (fertility impairment)
 - Serious organ toxicity at low doses
 - Structure and toxicity profiles that mimic existing drugs determined hazardous by the above criteria

ASHP, 1990; NIOSH, 2004

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Acute Exposure

- Lightheadedness
- Headache
- Dizziness
- Hair Loss
- Abdominal pain
- Nausea and vomiting
- Local skin or mucous membrane reactions
- Allergic reaction
- Nasal sores
- Contact dermatitis and eczema

Valanis et al, 1993; Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed.

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Delayed Exposure

- Reproductive risks
 - Fetal abnormalities
 - Spontaneous abortions
 - Menstrual cycle changes
 - Infertility
 - Miscarriages
 - Infertility, premature labor, low-birth weight, learning disabilities in offspring
 - Congenital abnormalities

Hemminki 1985; Strucker 1990; Shortridge 1995; Valanis 1997; Fransman 2007; Valanis 1999; Martin 2005; Ratner 2010

Cancer Risks

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Known carcinogens	Probable carcinogens
Arsenic	Azacitidine
Busulfan	Carmustine (BCNU)
Chlorambucil	Cisplatin
Cyclophosphamide	Doxorubicin
Melphalan	Mitomycin
Thiotepa	Nitrogen mustard
	Procarbazine
	Etoposide*

* Added 2012

IARC Website: <http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

Cancer Risks

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- Breast
- Colon
- Leukemia
- Lymphoma

Hemminki 1985; Strucker 1990; Shortridge 1995; Valanis 1997; Fransman 2007; Valanis 1999; Martin 2005; Ratner 2010

Recent Genotoxicity Studies

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- 2011: Evaluation of genotoxicity induced by exposure to antineoplastic drugs in lymphocytes of oncology nurses and pharmacists (El-Ebiary, et al)
- 2010: Chromosome 5 and 7 abnormalities in Oncology Personnel Handling Anticancer Drugs (McDiarmid, et al)

McDiarmid Study

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- Abnormalities detected in chromosome 5:
 - exposed versus non-exposed $p = .04$
- Increased incidence of chromosome 5 abnormalities seen with increased drug handling
 - Ratio 2.94, $p = .01$ all HDs
 - Ratio 8.54, $p = .01$ alkylating agents

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How Much Data Is There?

Contamination	Testing	# of studies
Environmental contamination	Wipe testing, air sampling	>20
Human uptake	Urinary drug excretion	15
Genetic damage	Chromosomal analysis Urine mutagenicity	>20

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Surface Contamination

- Many hospitals, clinics and offices are contaminated.
- Verified by wipe testing:
 - Can detect presence of drug on surfaces and be used as a benchmark
 - Not all drugs can be tested
 - Limited availability of labs to perform test
 - Can be expensive

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Wipe Testing



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Connor et al 2010

- Three University-based hospital cancer centers
- Study included wipe sampling of areas in and outside pharmacy, and urine collection from participants (n = 121)

Connor, T. et al. (2010). *JOEM*, 52(10)

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Connor et al 2010

3 sites combined

- 75% of pharmacy wipe samples were positive for at least 1 drug
- 43% of nursing wipe samples were positive for at least one drug
- Highest concentration found on the lid of a nursing disposal container
- 3 health care workers had positive urine tests

Connor, T. et al. (2010). *JOEM*, 52(10)

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Chu et al 2012

- Samples taken from 6 British Columbia hospital pharmacies
- Wipe test for Methotrexate and Cytosine before and after cleaning procedure
- 61% of the samples were positive before cleaning
- 56% of the samples were positive after cleaning

Chu, W. et al. (2012). *JOPP*, 18(1)

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Chu et al 2012

Site	Sample description	MTX (ng/cm ²)		CF (ng/cm ²)	
		Pre-clean	Post-clean	Pre-clean	Post-clean
A	Morning drug transfer tray (given to pharmacist from technician)	0.03	0.02	1.25	0.60
	Inside BSC on right side of prep cloth/drape	0.02	0.03	0.09	0.05
	Ledge of BSC in front of technician	1.11	0.26	4.17	0.76
	Handle of fridge in main pharmacy near pharmacist check area	ND	ND	0.29	0.13
B	Door handle inside cytotoxic drug preparation room	ND	0.01	0.22	0.23
	BSC surface where drug was prepared	12.45	0.33	7.18	1.29
	Door handle of drug pass-through cabinet in drug preparation room	ND	ND	0.10	0.03
	Metal tray in drug preparation room with prepared drugs on it	0.96	ND	2.32	0.10
C	Door handle inside cytotoxic drug preparation room	ND	ND	ND	0.03
	BSC surface	ND	ND	ND	ND
	Door handle inside chemo room	ND	ND	0.03	ND
	BSC surface	0.04	0.04	8.53	1.41
D	Blue pen on cart beside BSC	ND	ND	ND	ND
	Blue bins on shelves beside/behind BSC	ND	ND	0.05	ND
	Shelves between BSC and counter (where prepared drugs are placed in)	ND	ND	0.60	0.28
	Shaking machine beside main fridges	ND	ND	ND	ND
E	Metal tray on shelf seven (shelves between BSC and counter)	ND	ND	1.30	0.20
	Fridge door handle (small fridge beside counter)	ND	ND	0.06	0.03
	Black marker in BSC	ND	ND	ND	ND
	Scissors in BSC	ND	ND	ND	ND
F	BSC surface	ND	ND	ND	ND
	Pharmaceutical checking counter	ND	ND	ND	ND
	Chemotherapy metal tray	ND	ND	ND	ND
		ND	ND	ND	ND

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2 How am I at risk?

Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

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Contaminated Vials

Drug	# of vials checked	% of vials contaminated
Carboplatin	30	100
Cisplatin	6	33
Cyclophosphamide	140	75
Cyclophosphamide	100	100
Docetaxel	33	100
Doxorubicin	23	100
Doxorubicin	47	100
Etoposide	100	100
Fluorouracil	50	100
Ifosfamide	40	100

McDevitt et al, 1993; Sessink & Bos 1999; Connor 2005

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Drug Preparation



Everything inside this BSC is potentially contaminated with chemotherapy

Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

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Drug Preparation



Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

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Nursing Implications


- If the bag, syringe or tubing is contaminated when it leaves the pharmacy, it will contaminate **your** working environment.

McDevitt et al, 1993; Sessink & Bos 1999; Connor 2005

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Uptake Routes

- Most contamination occurs from skin contact
- Inhalation of aerosols and vapors can also occur under specific circumstances



Kromhout et al., 2000. Fransman et al., 2005, 2007


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Situations Where Exposure Occurs



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Bag puncture during transport



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Bedside Verification



Contamination can occur at any point prior to administration

Spiking At The Bedside

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Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

Priming IV Tubing

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Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

Syringes And Bags Are Not Closed

Syringes delivered with a standard "dead-head" can lead to a spill

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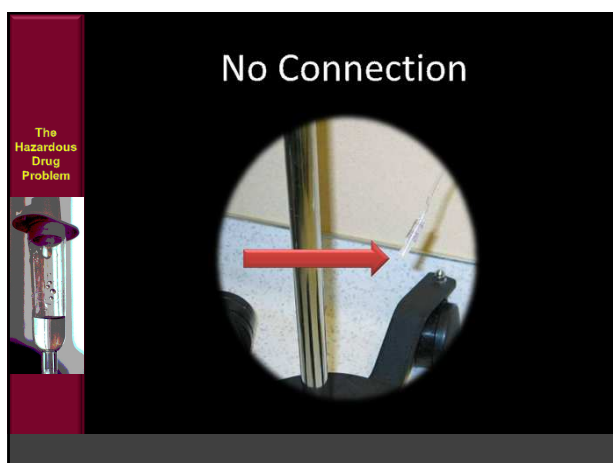
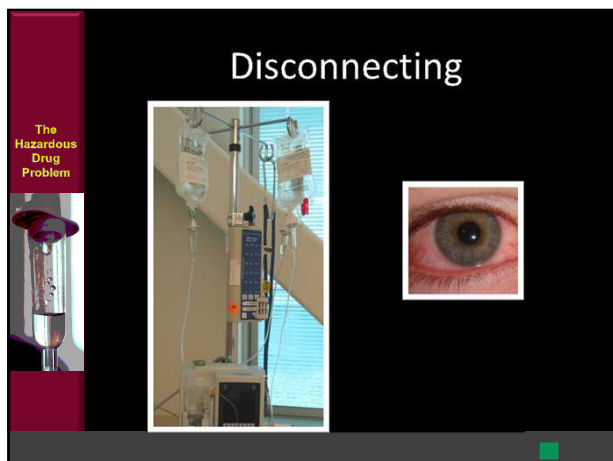
Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

Connecting

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Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed



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Wearing Improper PPE



Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

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Damaged Gloves



Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

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Inadequate Cleaning After A Spill



Alcohol and germicidal wipes do not inactivate hazardous drugs

Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

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During Disposal Of Excreta

- Unchanged drug and metabolites can be excreted in:
 - Urine
 - Feces
 - Emesis

Drug	Detected in urine
Carmustine	≥ 4 days
Cisplatin	≥ 5 days
Etoposide	≥ 5 days
Gemcitabine	≥ 7 days
Mitoxantrone	Up to 5 days

Polovich, 2011 "Safe Handling of Hazardous Drugs", 2nd Ed

3 What can I do to protect myself?

Follow the recommended guidelines

- **OSHA:**
 - Controlling Occupational Exposure to Hazardous Drugs
- **ASHP:**
 - Technical Assistance Bulletin / Guidelines on Handling Cytotoxic & Hazardous Drugs
- **ONS:**
 - Chemotherapy & Biotherapy Guidelines and Recommendations for Practice
- **APHON:**
 - The Pediatric Chemotherapy and Biotherapy Curriculum
- **NIOSH:**
 - Preventing Occupational Exposures to Antineoplastic & Other Hazardous Drugs in Healthcare Settings
- **USP:**
 - Chapter<797> Safe Handling Revision

OSHA (1986, 1995, 1999); ASHP (1985, 1990, 2006); ONS (1988, 1996, 1999, 2001, 2005, 2009, 2011); NIOSH Alert (2004); USP 797 (2008)

Compliance With Guidelines

Is Largely Voluntary




Compliance

- Compliance varies widely depending on:
 - Size and location of the institution
 - Workplace safety culture
 - Individual nursing education and experience
 - Staffing levels
 - Lack of equipment
 - Location of PPE

Polovich, M. & Clark, P., (2012). Oncology Nursing Forum , 39(3).

Barriers to Compliance

- Perceived immunity to risk
 - “It’s only a little chemo.”
 - “I’ve had plenty of exposure and I’m fine!”



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Compliance Surveys

- Ben Ami surveyed 61 oncology nurses in 2 hospitals
 - 67% did not believe chemotherapy could be absorbed through skin
 - 48% washed hands after administration
 - 94% consumed food or beverages in the drug preparation and administration areas

Ben Ami et al., 2001

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PPE Surveys

Martin & Larson 2003 (n=236)	Administration	Disposal
Gloves	94%	94%
Gowns	31%	26%

Polovich & Martin 2006 (n=330)	Administration	Disposal
Gloves	96%	96%
Gowns	52%	43%

MA Nursing Association 2007 n=400	Administration
Gloves	62%
Gowns	38%

2008 ONS Chemo SIG Survey*	Administration	Disposal
Gloves	94%	93%
Gowns	51%	45%

2010 Polovich (n=165)	Administration	Disposal
Gloves	78%	74%
Gowns	56%	53%

Martin & Larson, 2003 Oncology Nursing Forum 30(4); ; Polovich, M, & Martin, S. (2011). ONF, 38(6); Fuller T. (2007). JNEP4. Nov.

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Making It The Law

- In April 2011, the state of Washington passed legislation to adopt the NIOSH guidelines for all facilities handling hazardous drugs
- Similar legislation is pending in California and North Carolina

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3 What can I do to protect myself?

Adopt the Hierarchy Of Controls

Level 1
Elimination or substitution

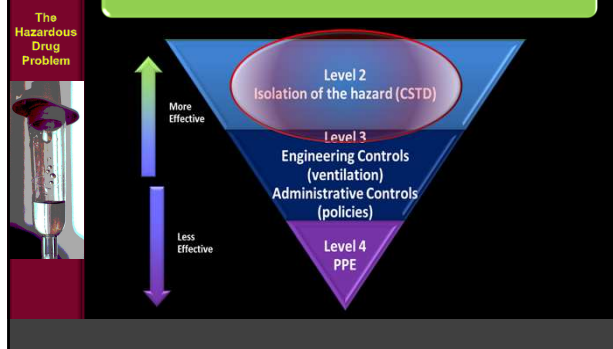
Level 2
Isolation of the hazard (CSTD)

Level 3
Engineering Controls (ventilation)
Administrative Controls (policies)

Level 4
PPE

*International Society of Oncology Pharmacy Practitioners <http://www.isopp.org/>

3 What can I do to protect myself?



Administration

Most exposure can be prevented by

1. Using a closed system transfer device (CSTD) (Level 2)
2. Using tubing setups which minimize exposure (Level 3)
3. Following policies and using proper technique (Level 3)
4. Wearing proper PPE (Level 4)



Time to rethink safety

"All possible means should be employed to prevent exposure. The use of a needle and syringe is no longer the safest way for us to be handling these agents."



Davis J, McLauchlan R, Connor TH. 2011

An Automotive Analogy

Two approaches to safety




A Pediatric Analogy

Two approaches to safety



Prevent accident
from occurring



Treating the
aftermath

Closed System Transfer Device (CSTD)

- Provides protection during drug preparation and administration by preventing the release of aerosolized and droplet chemotherapy

Closed System Transfer Device (CSTD)

- Recommended in the following US Guidelines:
 - 2006 ASHP Guidelines
 - 2008 USP <797> update
 - 2009 Chemotherapy and Biotherapy Guidelines
 - 2010 INS Guidelines
 - 2011 Safe Handling of Hazardous Drugs, 2nd Ed


Two Essential CSTD Components

1. A special vial adaptor used during drug preparation to prevent leakage of droplets and vapor
2. A closed valve used on tubing and syringes to prevent leakage before, during and after administration

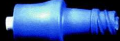
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Two Types of CSTD Designs

Membrane – to – membrane



Luer – to – Luer

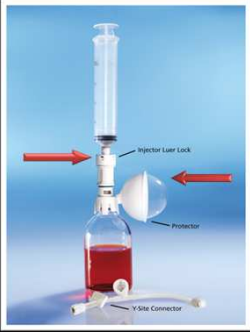


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PhaSeal®

(Carmel Pharma/BD)

- Membrane-to-membrane
- External chamber to trap vapors during drug prep
- Requires adaptors to use with luer devices
- Push-turn-push to engage internal needle




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ChemoCLAVE®

(ICU Medical)

- Needle-free Luer design
- Genie® has an internal balloon which Equalizes vial pressure during drug prep





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ChemoCLAVE®

(ICU Medical)

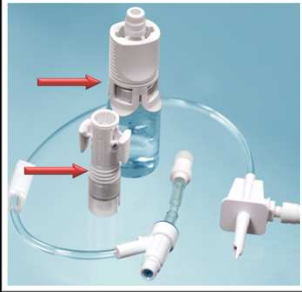
- Spiros® closed male luer uses Clave® components
- Internal valve is activated only after attaching to a luer device (e.g. Clave®)
- Valve remains closed until attached
- No adaptors required

OnGuard™
(B|Braun)

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- Membrane-to-membrane
- Dual-layer micro-filter
- Push on/pull off
- Requires adaptors for use with Luer devices



Texium® System
(Carefusion)

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- 0.2 micron vented filter on vial adaptor
- Closed male luer using SmartSite® components
- Compatible with SmartSite® components



Equashield
(Equashield Medical)

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- Membrane-to-membrane
- Dual-chamber syringe vent vapors back into rear of syringe
- Push on/pull off
- Not compatible with syringe pumps



Equashield
(Equashield Medical)

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- Requires adaptors for use with Luer devices



CSTD Syringe Connectors

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Other CSTD Benefits

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- Back-flushing
 - Saline syringe can be connected and disconnected for flushing HD from tubing without risk of contamination
- Dry spike
 - Hard plastic allows for “dry spiking” while preventing leaks and maintaining a closed system

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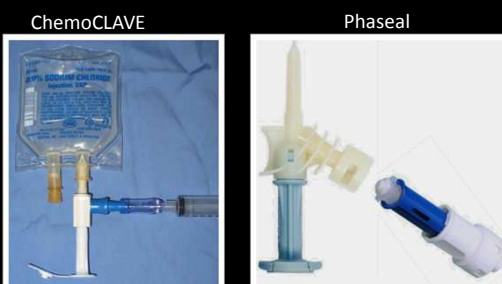
Dry Spikes

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Back-flushing

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Other CSTD Options

- Bags from pharmacy without tubings attached
- Closed luer-to-luer connections
- Eliminates the need to prime in BSC; no contaminated tubing



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Closed Systems Considerations

“If, in fact, the different closed systems currently available are equally effective, then the choice comes down to cost and ease of use.”

Davis, J., McLauchlan, R., & Connor, T. (2011). *JOPP* 17(1).

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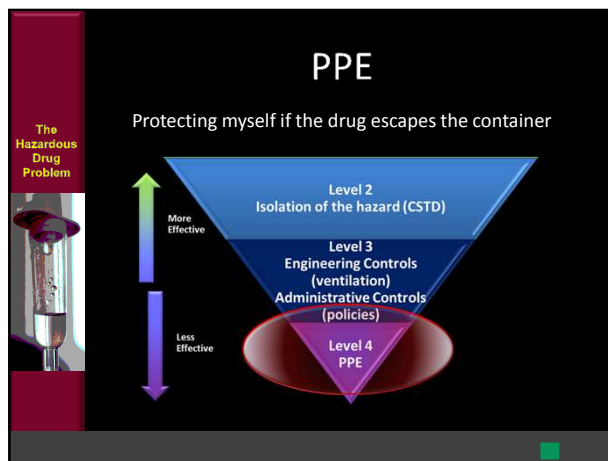
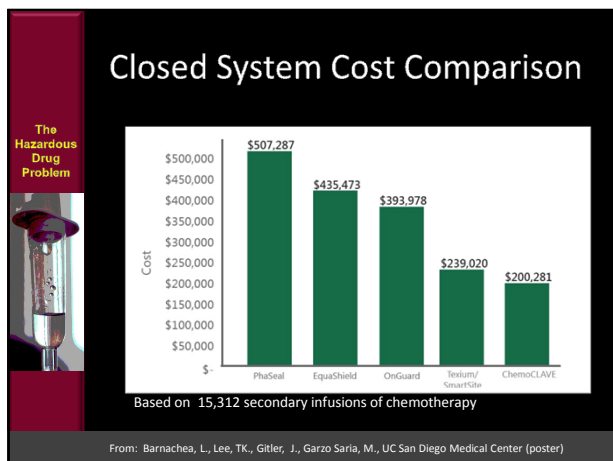
Ease Of Use

Compliance is directly related to ease of use:
If it is difficult to use, it won't get used.

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Conducting A CSTD Trial

- Evaluate
 - Ease of use
 - Amount of training required
 - Number of parts needed
 - Overall cost
 - Effectiveness



- ### Proper PPE
- The Hazardous Drug Problem**
- Chemotherapy-resistant gowns
 - Chemotherapy-resistant gloves
 - Eye protection should be available
 - Respiratory protection should be available in case of spill

- ### Wear PPE When
- The Hazardous Drug Problem**
- Preparing
 - Handling
 - Administering
 - Disposing
 - Cleaning of spills
 - Handling contaminated items
-
- Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, 2009.

Chemotherapy Gowns

"I don't think people who are buying gowns are checking to see what they are protecting against,"
 Luci Power, PharmD, Lead Author ASHP Guidelines (August 2012, ASHP News)

Chemotherapy drug tested
 Prevention Plus gowns are tested against the top chemotherapy drugs. See chart below.

The Prevention Plus Material has been tested against the following chemotherapy drugs per ASTM F739-99a:

• Dacarbazine	• Etoposide (Toposar)
• Carmustine (BiCNU)	• Paclitaxel (Taxol)
• Cyclophosphamide (Cytosan)	• Tlio-Taps
• Doxorubicin Hydrochloride	• Mitomycin C
• 5-Fluorouracil	• Vincristine Sulfate
• Cisplatin	

Test data available upon request

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Chemotherapy Gowns

- Polyethylene or vinyl coatings have been shown to resist chemotherapy
- Solid front with long sleeves and tight cuffs
- Single-use: not reapplied after removal

"Safe Handling of Hazardous Drugs", 2nd Ed; Harrison, BR & Kloos (1999). Penetration and splash protection of 6 disposable gown materials against 15 antineoplastic drugs. JOPP, 5.

Not acceptable
 Lab coats, or isolation gowns



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Gloves

- Effectiveness influenced by material, thickness and wear-time
 - Nitrile (latex-free rubber)
 - Latex
 - Polyurethane
 - Neoprene
- Long cuffs and powder-free
- 30 minute wear time
- Should meet the ASTM D6978 - 05 standard

Connor, 1999; Klein, 2003; Wallemacq, 2006; American Society for Testing and Materials

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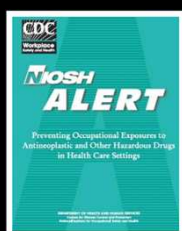
Gloves

- ASTM (6978-05) approved gloves have been tested against:
 - Carmustine
 - Cyclophosphamide
 - Doxorubicin
 - Etoposide
 - Fluorouracil
 - Paclitaxel
 - Thiotepa

Not All Gloves Are Equal

[illegible]

Double-Gloving



Gloves



Assess glove integrity before handling

Gloves

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- Wash hands thoroughly with soap and water after removal
- Alcohol gel is not effective for removing chemotherapy



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Eye Protection

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- Goggles or face shields should be readily available
- Used in situations where splashing could occur (e.g., bladder instillation)



Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, 2009.

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Respirators & Masks

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- Paper surgical masks are not effective for ANY chemotherapy
- NIOSH-approved respirator if risk of aerosol exposure
- Cartridge respirators are required for vapor exposure
- Both require fit-testing



Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, 2009.

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Vapors Vs. Aerosols

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- Carmustine
- Cisplatin
- Cyclophosphamide
- Etoposide
- 5-FU
- Ifosfamide
- Nitrogen mustard
- Thiotepa



Connor, T. et al. (2000); Kiffmeyer, T. et al. (2002)

Tubing Setups

- The type of tubing setup can affect the potential for exposure.



Bodily Fluids

- Use PPE when handling bodily fluids for a minimum of 48 hours
- 7 agents are highly excreted in urine:
 - Cyclophosphamide
 - Etoposide
 - Cisplatin
 - Dacarbazine
 - Fludarabine
 - Pentostatin
 - Methotrexate
- Place soiled linen, diapers, etc. in leak-proof bag

Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, 2009.

PPE > 48 Hours

Drug	Urine Detection (days)	Stool/Bile Detection (days)
Carmustine	4	-
Cisplatin	5	-
Docetaxel	-	7
Doxorubicin	5	7
Etoposide	5	-
Gemcitabine	7	-
Methotrexate	5	5
Vincristine	-	3
Vinorelbine	-	3

Safe Handling of Hazardous Drugs, 2011.

Double Flushing

- There is **no** evidence to support double-flushing in hospitals.
- However, it may be of some use with low volume toilets



Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, 2009.

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Body contamination

- Wash skin exposure immediately with soap and water
- Change clothing and put into chemotherapy bag
- Launder separately in detergent
- Complete appropriate documentation

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Resources

ONS Chemotherapy Special Interest Group Virtual Community

<http://chemotherapy.vc.ons.org/>

NIOSH Safety and Health Topic:
Occupational Exposure to Antineoplastic Agents

<http://www.cdc.gov/niosh/topics/antineoplastic/>

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