Importance of Aseptic Technique

TXCH Global HOPE

Texas Children's Hospital
CANCER AND HEMATOLOGY CENTERS

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Objectives

By the end of this presentation, the participant should be able to:

- Review the definition of pharmacy compounding
- Describe misadventures in pharmacy compounding which have shaped current practice and regulation
- Summarize the risks of preparing drugs in an environment without proper aseptic technique

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What is Pharmacy Compounding?

- The art and science of preparing custom medication orders which are not commercially available, such as:
  - Reconstituting a powder in bottle to prepare an oral suspension
  - Preparing a diluted solution for injection to facilitate
  - Reconstituting a lyophilized powder in vial to a specified concentration and adding to a base solution to create a specific dose and concentration
  - Preparing total parenteral nutrition
- Preparation of a dose by (or under direct supervision of) a pharmacist pursuant to an order from a licensed prescriber for an individual patient

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Definition of Aseptic Technique

- Aseptic= "free of germs"
- USP<797> defines aseptic technique as:
  - *"A set of methods used to keep objects and areas **free of microorganisms** and thereby **minimize infection risk to the patient**. It is accomplished through practices that maintain the microbe count at an irreducible minimum."*
- Process which protects the compounder, product, and patient

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Components of Appropriate Aseptic Technique

Protecting patients	Protecting healthcare professionals
• Protecting "critical sites" during preparation • Maintaining a clean environment • Wearing personal protective equipment • Washing hands • Following aseptic technique standard operating procedures	• Protecting "critical sites" during preparation • Maintaining a clean environment • Wearing personal protective equipment • Washing hands • Following aseptic technique standard operating procedures

The approaches are generally the same – emphasizing their importance!

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Medication Compounding Misadventures

1990
- 4 patients died of non-sterile, compounded cardioplegia solution
- 2 patients became blind from *P.aeruginosa* in compounded indomethacin eye drops

1998
- 11 children became septic from *E.cloacae* bloodstream infections from saline flushes

2001
- 11 patients contracted *S.marcescens* from compounded betamethasone injection
- 4 children developed *E.cloacae* bacteremia from compounded IV ranitidine

2002
- 5 patients were infected (1 died) with *Exophilia* from contaminated methylprednisolone injection
- Injectable baclofen and methylprednisolone were recalled by a pharmacy who detected *Penicillium, Methylobacterium*, and *Mycobacterium chelonae* in the final product

2003
- 19,000 patients with chronic lung diseases potentially exposed to *B.cepacia* detected in compounded inhalant solution

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Medication Compounding Misadventures

2004
- 36 patients developed Pseudomonas bacteremia from contaminated saline and heparin flushes

2005
- 25 patients were infected with *S. Marcescens* from contaminated magnesium sulfate bags
- 2 patients became blind from compounded ophthalmic injection which was contaminated with *P.aeruginosa* and *B.cepacia*
- 10 patients died from cardioplegia contaminated with gram negative rods

2011
- 16 adults developed severe eye infections from contaminated bevacizumab intraocular injections (one patient lost vision, another developed a CNS infection)
- 19 patients died from contaminated parenteral nutrition, predominantly with *S.marcescens*

2012
- 9 patients developed fungal endopthalmitis from compounded steroid and dye solutions
- >750 patients developed fungal meningitis (*Aspergillus* and *Exserohilum rostratum*) from contaminated methylprednisolone acetate injection (about 70 deaths)

And this is only the tip of the iceberg!

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Stability vs. Sterility

- A commonly misunderstood concept in healthcare
- A drug may be physically stable for many hours, days, weeks, or *months*… but it's STERILITY is much shorter
- Appropriate sterility dating goes hand in hand with proper aseptic technique
- ***Sterility often trumps stability***

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Beyond-Use Dating (BUD)

- Concept that recognizes the probability that a product may become contaminated even under ideal storage and handling conditions
- Contamination rates from batch preparation published in peer-reviewed literature: 0.3 – 16%
  - Ideally, this would be zero!
  - Optimally, BUD considers a target of <0.1% (1 contaminated dose per 1,000 prepared)
- BUD traditionally classified by the "risk level" of the compounded sterile product (CSP)

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CSP Risk Levels

Immediate use
- True emergencies (e.g., prepping a drip during a code), typically outside of a hood
- Must be a simple transfer of ≤3 commercially available agents, not more than 2 entries into a single container, no compounding for >1 hour, appropriately labeled, using aseptic technique

Low risk 12 hr
- Prep in a hood, but not in a formal cleanroom
- No hazardous drugs
- Must have SOPs for cleaning and environmental sampling

Low risk
- No more than 3 sterile drugs (including diluent), compounded in ISO class 5 hood in an ISO class 7 room
- Limited, basic, closed-system aseptic procedures
- Annual validation of room and staff

Medium risk
- 4 or more sterile ingredients with complex manipulations
- No bacteriostatic additive; product given over several days
- Multiple patient batching or multiple dose batching for a single patient

High risk
- Non-sterile ingredients or containers/equipement
- Made from sterile ingredients but less than ISO class 5 air
- Delay of >6 hours from compounding to sterilization
- Purity of contents is assumed but cannot be validated or verified

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BUDs of CSPs by Risk Level

These shorten based on the type of clean room and implementation of USP<800>

Risk Level	Room Temp (20 to 25ºC)	Refrigeration (2 to 8ºC)	Frozen Storage (-25 to -10ºC)
Immediate	1 hour	N/A	N/A
Modified Low*	12 hours	12 hours	N/A
Low	48 hours	14 days	45 days
Medium	30 hours	9 days	45 days
High	24 hours	3 days	45 days

**Modified Low = a risk level for a setting without ideal environmental controls for aseptic preparation; e.g., a contained segregated compounding area (ventilated hood, but no cleanroom) instead of ideal engineering controls*

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Remember!

Beyond use dating requires harmonization of STABILITY, STERILITY, and regulations on the preparation environment!

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Risks of Inappropriate Preparation and Dating

Patient related	Professional	Public
• Infectious complications • Meningitis, bacteremia, pneumonia, sepsis, death • Blindness, loss of vision	• Grief • Self-doubt • Exposure to potentially hazardous agents	• Distrust of the healthcare system • Impaired professional reputation

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Aseptic Technique: Implementation Steps

- Implement safe handling guidelines and procedures
- Establish beyond use dating guidelines for commonly used medications
- Ensure appropriate environmental controls are available for pharmaceutical compounding
- Design standard operational procedures *(e.g., environmental sampling, aseptic technique validation)*

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