Importance of Aseptic Technique

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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

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

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

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***

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)

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

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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