Drug Shortages: the good, the bad and the ugly
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Presentation Objectives
1. Review the lifecycle of a drug shortage from cause to effect
2. Describe how drug shortages have led to unsafe practices and increased risk of errors
3. Examine best practice responses to announced and unannounced drug shortages at a large non-profit community hospital

Disclosure
I have nothing to disclose. I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity or any affiliation with any organization.

Drug Shortage Defined
- "A supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent"
- "Products used to prevent or treat a serious or life-threatening disease or medical condition for which there is no other available source with sufficient supply of that product or alternative drug available"

Good
- Job security
- Improved collaboration & communication
- Clinicians choose who receives product in stock

Bad
- At the mercy of manufacturers
- Amount and extent increased
- Compromised or delayed therapy

Ugly
- Clinicians choose who receives product in stock

Impact of Drug Shortages
- Increased risk of errors
- Unsafe practices
- Compromised therapy
- Delayed therapy
- At the mercy of manufacturers
**National New Shortages by Year**

January 2001 to March 2018

<table>
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<tbody>
<tr>
<td>New shortages</td>
<td>135</td>
<td>85</td>
<td>73</td>
<td>56</td>
<td>74</td>
<td>29</td>
<td>59</td>
<td>129</td>
<td>146</td>
<td>104</td>
<td>211</td>
<td>221</td>
<td>184</td>
<td>220</td>
<td>247</td>
<td>304</td>
<td>406</td>
<td>73</td>
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**Active and Ongoing Shortages**

Five Year Trend

<table>
<thead>
<tr>
<th>Q1-2013</th>
<th>Q1-2014</th>
<th>Q1-2015</th>
<th>Q1-2016</th>
<th>Q1-2017</th>
<th>Q1-2018</th>
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<tbody>
<tr>
<td>295</td>
<td>305</td>
<td>265</td>
<td>185</td>
<td>176</td>
<td>202</td>
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</tbody>
</table>

**Common Drug Classes in Short Supply**

National Drug Shortages: Common Drug Classes in Short Supply (Through March 31, 2018)

- Antimicrobials: 29
- Chemotherapy: 15
- Cardiovascular: 15
- Central Nervous System: 32
- Electrolytes, Nutrition: 37

**Drug Shortages: Top Five Classes**

<table>
<thead>
<tr>
<th>Class</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
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</thead>
<tbody>
<tr>
<td>Antimicrobials</td>
<td>29</td>
<td>15</td>
<td>15</td>
<td>32</td>
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<tr>
<td>Chemotherapy</td>
<td></td>
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<td></td>
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<tr>
<td>Cardiovascular</td>
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<tr>
<td>Central Nervous System</td>
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<tr>
<td>Electrolytes, Nutrition</td>
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</table>

**Underlying Causes**

- Manufacturing Difficulties (30%)
- Supply and Demand (8%)
- Shortage of Raw and Bulk Materials (2%)
- Natural disasters (3%)
- Discontinuation (4%)
- Unknown (33%)

**Natural Disasters**

- 1998-Hurricane George: Nitroglycerin 0.3 mg
- 2005-Hurricane Katrina: Access to medications via hospitals, clinics and pharmacies
- 2017-Hurricane Maria: IV saline bags, Levothyroxine, Amino acids
Puerto Rico Manufacturing Plants

- One of the world’s largest centers for pharmaceutical manufacturing
- 11 of the top 20 prescription meds sold in the US are manufactured in P.R.
- Responsible for producing 10% of all pharmaceuticals consumed in the US

Damage from Hurricane Maria and continued issues with power outages have decreased manufacturing and led to shortages around the world.

- IV saline bags
- Amino acids
- Levothyroxine

AbbVie  AstraZeneca  Bristol-Myers Squibb  Merck
Amgen  Baxter  Eli Lilly  Pfizer

Shortage Example: Propofol

Timeline

Pharma Activities

2009  Three manufacturers (Teva, Hospira, APP)

early Oct 2009  Hospira recall (contamination)

late Oct 2009  Teva recall (contamination)

APP becomes sole supplier (FDA allowed APP to import and distribute alternative)

May 2010  Teva announced departure from market

Jul 2010  Hospira pending return to market

The Bad

Increased Labor Cost
Delays in Clinical Trials
Medication Errors
Lack/Less Effective alternatives
Surgical delays
Increased Drug Cost/Hospital Expenses
Adverse Effects

How have drug shortages led to unsafe practices and increased risk of errors?

Impact of Drug Shortages

Effects on Patient Care Caused by Drug Shortages: A Survey

- Electronic survey to 1,516 Directors of Pharmacy
- 6 domains:
  - Demographics
  - Adverse events
  - Medication errors
  - Outcomes
  - Patient complaints
  - Institutional cost

- 193 respondents (13%)
- Range between 1 and 10 medication errors

Impact of Drug Shortages

Patient Outcomes Caused by Drug Shortages

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Individual N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternative medication used</td>
<td>146 (85.3)</td>
</tr>
<tr>
<td>Delay of therapy</td>
<td>121 (70.8)</td>
</tr>
<tr>
<td>Increased patient monitoring</td>
<td>84 (49.1)</td>
</tr>
<tr>
<td>Suboptimal treatment</td>
<td>83 (48.5)</td>
</tr>
<tr>
<td>Increased length of hospitalization</td>
<td>56 (32.7)</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>27 (15.8)</td>
</tr>
<tr>
<td>Patient transferred to institution with a supply of medication</td>
<td>21 (12.3)</td>
</tr>
<tr>
<td>Re-admission caused by treatment failure</td>
<td>15 (8.8)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (1.2)</td>
</tr>
</tbody>
</table>

Impact of Drug Shortages

Med Errors Caused by Drug Shortages

- Omission
- Wrong Dose Dispensed/Administered
- Wrong Drug Dispensed/Administered
- Wrong Frequency
- Wrong Route
- Wrong Indication
- Other*
The impact of drug shortages on patients with cardiovascular disease: causes, consequences and call to action
Am Heart J 2016;175:130-41

Critical drug shortages: implications for emergency medicine
Academic Emergency Medicine 2014; 21:704-711

<table>
<thead>
<tr>
<th>Medication</th>
<th>Shortage</th>
<th>Cause</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>Contamination with manufacturer in China</td>
<td>Serious injuries and death</td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>Contamination with (oversulfated chondroitin)</td>
<td>149 deaths in 11 countries (81 in US)</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>Concentration 50mg/mL substituted for 10mg/mL, improperly diluted</td>
<td>Overdose-confusion and delirium</td>
<td></td>
</tr>
</tbody>
</table>

Increased Risk for Errors
- Unknown conversion factors
- Multi-dose vials for single dose vials
- Premixed bags replaced with vials
- Varying alternative options
  - Furosemide
  - Benzodiazepine
  - Morphine
  - Hydralazine
  - Diltiazem
- Incorrect Protocol/Dose
  - Cisatracurium, vecuronium and pancuronium

Increased Risk for Errors
- Lack antimicrobial retardant in alternative product
- Counterfeit medications from unfamiliar/alternative sources
- Decrease in supply of alternative agents
  - morphine-hydmorphone, furosemide-torsemide-bumetanide
- Compounding errors
- Use of unfamiliar ingredient
- Alternatives or concentrations not programmed in drug library
- Death

Alternative Route/Formulation
- IV Bolus
  - Aztreonam
  - Cefazolin
  - Cefepime
  - Ceftriaxone
  - Clindamycin
  - Nafcillin
  - Vancomycin
- Vial to Bag
  - Protonix
  - Frozen formulation
  - Piperacillin/Tazobactam

Epinephrine Kits
- Backordered!

Best Practices
- How can your hospital better manage shortages
How Can Your Hospital Better Manage Shortages

“How receiving and communicating accurate and complete information is critical to managing a drug shortage.”

Yen Nguyen, PharmD, Senior product manager, Pharmacy Solutions, McKesson Health Systems

Drug Shortage Leading to Serendipitous Adoption of High-Value Care Practice

Within 3 days:
- Automated message advising limiting the use of intravenous PPI to patients with active upper gastrointestinal bleeding
- All remaining intravenous PPI orders required pharmacy approval prior to execution
- Automatic stop orders after 24 hours of intravenous PPI with a step down to oral PPI


Assessment

Preparation

Contingency

Determine next option when a product is unavailable


John Hopkins Bayview Medical Center (JHBMC)

Drug Shortage Task Force

- Clinical pharmacy specialists
- Front line staff, pharmacists
- Pharmacy administration
- Pharmacy buyer
- Pharmacy system administrator
- Non-pharmacy content experts (cardiology, nephrology)

Early identification of shortage

Allocation tactics and conversation strategies

Insight from affected stakeholders

Identification of alternative agents or therapies

JHMC Key Elements of Success

- Clear expectations of each member of the drug management team
- Early identification of medication shortages, real-time inventory and usage data, and identification of alternative agents
- Effective communication strategies to all individuals affected by shortage situation
- Identification of key stakeholders for each shortage
- Real-time implementation of conservation and management plans, including modifications of computer order entry systems

Memorial Regional Hospital

- Drug shortage team
  - Automation and systems manager
  - Pharmacy buyers
  - Pyxis administrators
  - Clinical and operations managers
  - Clinical Coordinators
  - Director of Pharmacy
- Daily, morning shortage huddles
- Weekly system-wide drug shortage meetings
- Internal shortage link with database
- Communication via internal huddles three times per day

Policy and Procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Department Approval and Date: Director of Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Staff Approval Date: Pharmacy District-wide</td>
<td></td>
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<tr>
<td>Title: Handling Manufacturer Back Orders and Shortages</td>
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Purpose: To standardize the process for handling medications on backorder or in short supply

PROCEDURE:
1. Within the pharmacy, the pharmacy buyer or pharmacist in charge may direct the pharmacy buyer or pharmacist in charge to contact the manufacturer for additional supplies
2. The pharmacy buyer or pharmacist in charge will determine if additional supplies are available based on departmental utilization and anticipated release dates
3. The pharmacy buyer or pharmacist in charge will notify the appropriate pharmacy buyer or pharmacist in charge of any additional supplies
4. The pharmacy buyer or pharmacist in charge will report any additional supplies to the appropriate pharmacy buyer or pharmacist in charge

SharePoint

- Drug Shortages
- Drug Procurement and Inventory Management
Micafungin Shortage

Wednesday

• Buyer notified pharmacy management team of micafungin shortage
• Six active patients

Thursday

• Requested allocation of micafungin
• Total stock depleted and actual count inaccurate
• Caspofungin unavailable

Friday

• Collaborated with medical staff, pharmacy and nursing
• Anidulafungin made available for formulary use

Conversion of 250 mL bag to 100 mL bag

Admix 250 mL to 100 mL

Tranexamic Acid Use During Aminocaproic Acid Shortage

Additional Measures

• Reserve 100 mL normal saline bags for insulin drips and cardiac products
• Explore other concentration options
• Develop slow IV bolus over 5 minutes program education for nursing
• Secure Baxter frozen antibiotic alternatives
• Update order sets to include the new medications and slow IV bolus entries
• Update smart pumps to accommodate Baxter frozen concentrations and other concentrations
Maximize Safety

- Stay informed
- Monitor stock
- Triage usage
- Communicate with clinicians
- Evaluate safe alternatives and/or restrictions
- Identify safety issues
- Report medication errors and near misses

Drug Shortage Apps

- FDA launched a mobile phone application (app) specifically designed to speed public access to valuable information about drug shortages
- Identifies current drug shortages, resolved shortages, and discontinuations of drug products, the agency notes

What We've Learned

- Proactively identify alternatives for shortages
- Prepare alert in advance for anticipated shortages
- Individualize communication (i.e. nursing, medical staff, pharmacy)
- Verify stock manually with automated inventory management
- Remove alert when shortage subsides
- Remove non-formulary option for temporary alternatives
- Provide instructions and/or add to drug library

What We've Learned

- Continuous surveillance is key
- Collaborate and share with other hospitals
- It requires a designated, full time team
- Changes occur within the hour, day to day
- Overall process is a team effort

What We've Learned

- Our shortage king and entire team need a vacation!

Additional Resources

- ASHP Resource Center: www.ashp.org/shortages and www.ismp.org/sc?id=3076
- FDA Drug Shortages Page: www.ismp.org/sc?id=3071
- US Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response: www.ismp.org/sc?id=3072
- ISMP newsletter on managing drug shortages: www.ismp.org/sc?id=241
**Additional Resources**

- ISMP newsletter on managing drug shortages: [www.ismp.org/sc?id=241](http://www.ismp.org/sc?id=241)
- ASHP and University of Utah guidance on small-volume parenteral solutions shortages: [www.ismp.org/sc?id=3073](http://www.ismp.org/sc?id=3073)
- Centers for Disease Control and Prevention guidance on vaccines in short supply: [www.ismp.org/sc?id=3074](http://www.ismp.org/sc?id=3074)
- American Society for Parenteral and Enteral Nutrition guidance on shortages with parenteral nutrition components: [www.ismp.org/sc?id=3075](http://www.ismp.org/sc?id=3075)

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**Final Thoughts**

- New shortages have declined
- Prescribers are more vigilant
- Healthcare systems are leveraging resources

- Disruptions and uncertainty in supply
- Expensive, critical medications can't be administered without fluids

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**References**