Antidote Stocking Guidelines and Practical Tips

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- Project was supported by multiple companies
  - Cumberland Pharmaceutical
  - EMD
  - Fougera
  - Heyltex
  - Protherics
  - Rare Disease Therapeutics

What is an Antidote?
- Antidote ≠ Anecdote
- An antidote is a substance that when injected into a patient...
- Produces a publication

Why Stock Antidotes?
- The Joint Commission
  - MM 2.10: Medications for dispensing or administration be selected, listed, and procured according to criteria.
  - MM 2.30: Emergency medications or supplies, if any, be consistently available, controlled, and secured.
- State government
  - California hospital sanctioned for violating regulation requiring “availability of prescribed medications 24 hours a day”
  - Digoxin Fab was not available immediately for patient with cardiac glycoside toxicity

Insufficient Antidote Stocking is Widespread

<table>
<thead>
<tr>
<th>North America</th>
<th>International</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona, 1991</td>
<td>Taiwan 2000</td>
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<tr>
<td>New York, 1994</td>
<td>France (SAMU) 2001</td>
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<tr>
<td>Tennessee, 1994</td>
<td>Norway 2002</td>
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<tr>
<td>Massachusetts, 1997</td>
<td>Quebec, Canada 2003</td>
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<tr>
<td>Ontario, Canada 2001</td>
<td>British Columbia 2003</td>
</tr>
<tr>
<td>Philadelphia, 2001</td>
<td>Czech Republic 2003</td>
</tr>
<tr>
<td>Illinois, 2007</td>
<td>British Columbia 2005</td>
</tr>
<tr>
<td>Others</td>
<td>North Palestine 2006</td>
</tr>
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<td></td>
<td>Spain 2006</td>
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</tbody>
</table>

Inadequate Pyridoxine Stock and Its Effect on Patient Outcome

Anthony M. Buda, BSPharm,1 Todd Sigg, PharmD,1 Danish Haque, MD,1 and Christina Hornsby Fandley, MD1

- Status epilepticus after 9 g INH - Hospital had only 1 g pyridoxine
- 4 g obtained from another facility, but refractory seizures continued. Treated with large doses of benzodiazepines and emergent hemodialysis
- Eventually, 5 g of pyridoxine tablets via nasogastric tube

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EXPERT CONSENSUS GUIDELINES FOR HOSPITAL STOCKING OF EMERGENCY ANTIDOTES IN THE UNITED STATES

Antidote Summit Method Overview

Phase 1. Literature collection and analysis
MedLine, Major Textbooks, Panel Citations

Primary Reviewer
Standardized Format

Phase 2. Expert consensus panel
19 persons - diverse perspectives

Consensus
75%, no strong disagreement

Expert Consensus Panel

Stephen Borron, MD, MS
E. Martin Caravati, MD, MPH
Dan Cobaugh, PharmD
ASHP Foundation
Steven Curry, MD
Jay L. Falk, MD
Lewis Goldfrank, MD
Susan Gorman, PharmD, MS
CDC Strategic National Stockpile
Stephen Groft, PharmD
Director, NIH Rare Diseases
Kennon Heard, MD
Ken Miller, MD, PhD
Orange County Fire & NAEMSP
Kent R. Olson, MD
Gerald O’Malley, DO
Donna Seger, MD
Steven Seifert, MD
Marco Sivilotti, MSc, MD
Tammi Schaeffer, DO
Anthony J. Tomassoni, MD, MS
Robert Wise, MD
VP - The Joint Commission

Discipline/Specialty Participants

Clinical Pharmacology 3
Critical Care 3
Clinical Pharmacy 2
Disaster Prep/Response 6
Emergency Medicine 11
EMS 4
Hospital Pharmacy 1
Internal Medicine 2
Clinical Toxicology 15
Pediatrics 2
Poison Center Admin 9
Public Health 1
Regulatory Medicine 4

Antidote Indication

Recommendation

Should Be
Available within
60 Minutes
Immediately
Available

Class of Evidence

Total of 28 Medications

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### Antidotes: Immediately Available

1. Atropine
2. Crotaline snake antivenom
3. Coral snake antivenom
4. Cyanide antidote
5. Digoxin immune Fab
6. Flumazenil
7. Glucagon
8. Methylene blue
9. Naloxone
10. Physostigmine
11. Pyridoxine
12. Sodium bicarbonate

### Antidotes: Available within 1 hour

1. Acetylcysteine
2. Calcium chloride
3. Calcium gluconate
4. Cyanide antidote
5. Deferoxamine
6. Dimercaprol
7. Ethanol/fomepizole
8. Octreotide
9. Potassium iodide
10. Pralidoxime
11. “Immediately available list”

### Antidotes: Stocked, but no time limit

1. Black widow spider antivenom
2. EDTA
3. DTPA
4. Prussian blue

### Antidotes: Need not be stocked

1. Botulism Equine Trivalent Antitoxin
2. Botulism immune globulin (BabyBIG)

### How Much Antidote Should Be Stocked By Hospital

- **Amount needed for 1 patient**
  - 8 hours, 24 hours (AWP: $70,000, $90,000)
  - Some synthesis by the panel was needed
    - Acetylcysteine
      - 8 hours – 28 grams
      - 24 hours – 56 grams
  - Hazard Vulnerability Assessment
    - The Joint Commission
    - Some hospitals have uneven stocking

### It's more than just the antidote

- Patient
- Evaluation
- Re-evaluation
- Treatment

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Hazard Vulnerability Analysis

- Hospitals not all the same
- Hazard vulnerability assessment required by TJC
- “Identification of potential emergencies and the direct and indirect effects these emergencies may have on the hospital’s operations and the demand for its services.”


<table>
<thead>
<tr>
<th>Factor</th>
<th>Principle</th>
<th>Example</th>
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<tbody>
<tr>
<td>History or experience of use</td>
<td>Some modes of suicide or abuse become locally prevalent</td>
<td>Popularity of cyanide or other specific agents as a suicide agent</td>
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<td></td>
<td></td>
<td>Amateur snakekeepers (e.g. cobras) in area</td>
</tr>
<tr>
<td>Anticipated volume of use</td>
<td>More than 1 victim of a poisoning may occur</td>
<td>Residential/commercial fires</td>
</tr>
<tr>
<td>Anticipated time to re-stocking of antidote</td>
<td>Time to re-stocking varies among hospitals</td>
<td>Multiple casualty incidents (smoke inhalation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indigenous snakebite in areas with frequent occurrences</td>
</tr>
</tbody>
</table>

Why?

- Cost
- Medical ignorance
- Antidotes used infrequently
- Everyone responsible = no one responsible
- Lack of guidance

Conclusions

- Antidote non-stocking is common
- Recommendations can help reduce insufficient treatment of poisoned patients
- Analysis – What antidotes and when are they needed?