Is the Drug Shortage Affecting Patient Care in Your Critical Care Unit?

Sporadic shortages of various pharmaceutical products in the United States are nothing new. But since the early 1990s, the prevalence, scope and negative repercussions of these shortages have escalated to critical levels, prompting not only heightened monitoring, but increasingly louder alarms regarding this already lethal problem. Just over the past few years, the number of drugs identified as in short supply or as completely unavailable has multiplied more than 6-fold from a 2006 total of 561 to more than 230 in 2011, with some knowledgeable sources projecting a sum of 360 drugs by the end of 2011, the highest number in history. In addition, a number of the medications listed as scarce or unavailable during 2010 remained locked in those categories throughout 2011.

Definition of a “Drug Shortage”

The Drug Shortage Program (DSP) at the Food and Drug Administration (FDA), Center for Drug Evaluation and Research, defines a drug shortage as “a situation in which the total supply of all clinically interchangeable versions of an FDA-regulated drug is inadequate to meet the current or projected demand at the user level.” The DSP is primarily concerned with shortages of medically necessary drugs that have a significant effect on public health.

In 2001 the American Society of Health-System Pharmacists (ASHP) created the Drug Product Shortages Management Resource Center (www.ashp.org/shortage) for information related to drug shortages. This site, managed by the University of Utah’s Drug Information Service (DIS), maintains the most comprehensive list of scarce or unavailable drugs. The DIS defines drug shortages from the point of view of a health care organization as

a supply issue that affects how the pharmacy department prepares or dispenses a product or influences patient care when prescribers must choose an alternative therapy because of supply problems.

These differing definitions of what constitutes a drug shortage explain why the data reported by these sources may display different absolute numbers, yet comparably illustrate the same equally troubling trends (see Figure).

Drugs in Short Supply

An ASHP list (see Table) show these shortages primarily affect sterile injectables, including many of the more established and relatively inexpensive chemotherapeutic agents. In addition, however, increasing numbers of anesthetics, analgesics, antibiotics, sedatives, and the vitamin and electrolyte additives necessary for intravenous feedings are in scarce supply. The list of commonly administered critical care medications in scant or no supply is striking: amiodarone, atropine, diazepam, digoxin, diltiazem, dopamine, epinephrine, furosemide, heparin, labetalol, lidocaine, morphine, and norepinephrine. Many of these therapies are not only mainstays but essential to optimal patient care.
Effects of the Drug Shortage

Repercussions from these drug shortages cut a wide path of challenges and problems, adversely affecting patients, providers, health care institutions, and research programs.

Patients

The adverse outcomes of drug shortages to patients that have already been identified are far-reaching and increasingly detrimental, ranging from mere annoyances to mortal consequences:

Delays or Cancellation of Treatments or Surgery. When established therapies for managing certain disorders are not available, care may be deferred or postponed until supply of that product resumes. A 2011 analysis of 228 hospital and pharmacy professionals found that 80% had experienced drug shortages that led to delays or cancellation of patient interventions.

Substandard Care. If drugs widely accepted as the optimal therapy or best available for treating a specific condition are no longer available and no comparable alternatives exist, the patient may receive a substitute product that is known or anticipated to be less effective, rather than receiving no treatment at all.

More Expensive Care. As one might expect with high demand for products in short supply, the current drug shortage has precipitated a secondary “grey market,” where middlemen from nontraditional sources sell drugs, particularly lifesaving drugs, at premium prices. At times, health care facilities find themselves in the position of needing to make do with pharmaceutical products that are both more costly and less effective.

Compromised Patient Safety. An analysis of 228 hospital and pharmacy staff reported that 89% of facilities experienced shortages associated with compromised medication safety or errors in patient care. One factor contributing to patient safety concerns arises when a substitute drug must be used in place of the customary product and requires changes in dosage strength or dosage form—the need for those adjustments may heighten the risk of errors. Other safety issues arise if the substitute drug carries different side effects or allergic or synergistic reactions than the previous therapy.

If alternative drugs are obtained via one of the grey market vendors, additional safety concerns escalate, owing to the inability to ensure that all regulations and standards have been followed and that the traditional pharmaceutical supply chain of custody has not been compromised at any point. If suppliers other than reputable pharmaceutical distributors are providing drugs, the patient may pay both an inflated as well as the ultimate price if the integrity of those drugs is unknown.

Complications. As mentioned, delays or postponements of treatments or surgical procedures as well as unanticipated side or untoward or allergic effects of substitute medications may contribute to the development or worsening of clinical complications, particularly among patients who are already immunocompromised or critically ill, very young or very old.

Increased Length of Stay. Any and all delays, postponements, and/or cancellations of treatments or surgical procedures can lead not only to complications but prolong the duration of patients' hospitalizations.

Death. A recent review of the health care industry found that at least 15 deaths over a 15-month period were attributed to drug shortages, owing to either the right drug not being available or to dosing errors or related problems in preparation or administration of alternative medications. The most egregious case...
involved a shortage of sterile liquid ingredients of a tube feeding. The deaths occurred as a result of bacteria from the water spigot used to rinse the container that contaminated the stirrer and container used to mix the formula. As a result, 19 patients developed a bacterial infection from the feeding and 9 of those patients died.

Providers

Drug shortages also take a toll on health care providers, primarily pharmacologists, pharmacists, and physicians. Pharmacy professionals may need to spend time searching and negotiating for dwindling supplies of drugs that continue to evaporate with no guarantees of success. Additional hours must also be usurped, assisting physicians and nurses in selecting the best alternatives when the drug of choice is not available.

Physicians and other care providers must redirect their therapeutic efforts from applying the known optimum therapy to postponing and rescheduling surgery or other therapeutic modalities in addition to searching and sifting through alternative forms of treatment.

Table: American Society of Health-System Pharmacists’ current drug shortage list

<table>
<thead>
<tr>
<th>Acetazolamide injection</th>
<th>Doxycycline hyclate injection</th>
<th>Milrinone injection</th>
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<tr>
<td>Acetylcysteine inhalation solution</td>
<td>Droxidopa injection</td>
<td>Mitomycin injection</td>
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<td>Acyclovir injection</td>
<td>Epinephrine metered dose inhaler</td>
<td>Morphine injection</td>
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<td>Amikacin injection</td>
<td>Epinephrine injection</td>
<td>Multiple vitamins for infusion</td>
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<td>Aminocaproic acid injection</td>
<td>Esmolol injection</td>
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<td>Etomoxide injection</td>
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<td>Amoxicillin injection</td>
<td>Flunoxamide injection</td>
<td>Neostigmine methylsulfate injection</td>
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<td>Arginine 10% injection</td>
<td>Foscarnet injection</td>
<td>Nicardipine hydrochloride injection</td>
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<td>Ascorbic acid injection</td>
<td>Furosemide injection</td>
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<td>Atropine sulfate injection</td>
<td>Gentamicin capsules</td>
<td>Paclitaxel injection</td>
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<td>Azithromycin injection</td>
<td>Gliclazide injection</td>
<td>Pancuronium injection</td>
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<td>Bleomycin injection</td>
<td>Glycopyrrolate injection</td>
<td>Papaverine injection</td>
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<tr>
<td>Bupivacaine with epinephrine injection</td>
<td>Heparin Sodium injection</td>
<td>Pargoranic acid</td>
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<td>Buprenorphine injection</td>
<td>Hyaluronidase injection</td>
<td>Phentolamine injection</td>
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<td>Calcium chloride injection</td>
<td>Hydralazine injection</td>
<td>Phenyletox injection</td>
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<td>Calcium gluconate injection</td>
<td>Intravenous fat emulsion</td>
<td>Phytomenadione (vitamin K) injection</td>
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<td>Carprofen injection</td>
<td>Ketoconazole solution</td>
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<td>L-Carnitine fumarate injection</td>
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<td>Methylene blue injection</td>
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<td>Methyldopate hydrochloride</td>
<td>Torsemide injection</td>
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<td>Valproate sodium injection</td>
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<td>Vitamin A injection</td>
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<td>Zinc injection</td>
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*As of November 13, 2011. Partial listing; for a complete list go to www.ashp.org/DrugShortages/Current/#.

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Hospitals

In June 2011 both the ASHP and the American Hospital Association (AHA) surveyed their respective members regarding the drug shortage. The ASHP survey found that annual labor costs nationwide to manage drug shortages were estimated at $216 million.1 The AHA surveyed some 820 hospitals to assess the impact of drug shortages on patients and hospitals over the previous 6 months. Striking findings included18:

- 99.5% of hospitals experienced one or more drug shortages
- 44% of hospitals reported 21 or more drug shortages during that brief time
- All treatment categories reported drug shortages
- More than 50% reported not always being able to provide recommended treatments
- 78% reported the need to ration or restrict drugs
- 92% reported increased drug costs due to the need to purchase more expensive alternatives from new sources

The additional cost burden likely to befall US hospitals annually from the purchase of more expensive substitutes and for the related enhanced labor cost is currently projected to reach $415 million,4 largely attributable to price gouging within the grey market, where markups average 650% above normal prices,3 especially for drugs used to treat critically ill patients14,15 and those needing anesthesia for surgery. One example from a 2011 Buyer Beware report3 describes a vendor offering to sell the generic antihypertensive drug labetalol for $1200, a stunning 4533% markup from its customary cost of $25.90 per dose. Although this was the single highest recorded markup at that time, other proportionately greedy heists were also uncovered3:

- Labetalol, 4533%
- Propofol, 3161%
- Papaverine, 2979%
- Protamine, 2752%
- Levophed, 2642%
- Sodium chloride concentrate, 2350%
- Furosemide injection, 1721%

Research

The chemotherapy drugs most affected by the shortage are essential components in established therapy either alone or in combination with other newer products for numerous research trials. The Coalition of Cancer Cooperative Groups recently reported19 that nearly half of all ongoing clinical cancer trials require chemotherapeutic agents that are now vanishing. As a result, the efficacy of current approaches to manage many forms of cancer cannot be determined and future directions in this work are left suspended. Not just data and clinical evidence, but lives are being lost.

Causes of Drug Shortage

Many interrelated and multifactorial trends have converged as contributors to the current drug shortage. These trends may be grouped into 3 categories: regulatory, economic, and health care.

Regulatory

- According to the FDA,11,20 the primary cause of the shortages is production shutdowns due to manufacturing disruptions related to problems such as ingredient microbial contamination and impurities or foreign particulates present in medicines that prevent product quality from meeting FDA standards and regulations.12,13 A recent report found that more than 40% of sterile injectable drug shortages in 2010 were attributable to substandard product quality issues of this nature.13
- When regulatory actions lead to production delays, FDA rules and procedures create disincentives that prevent other drug makers from stepping in to provide drugs in short supply. It is expensive to launch production of a generic drug and FDA manufacturing approval for a generic drug can require 2 1/2 years.2,10
- Drug manufacturers are not required to give advance notification to either customers or the FDA when they plan to stop producing a medicine, so competitors have no means to respond to a potential scarcity of the drug.
- Drug recalls4
- Medicare price controls enacted in 2003 and in effect since 2005 have hamstrung the customary free market forces when shortages arise for products in high demand by limiting price increases for drugs sold to hospitals and physicians (vs directly to the public) and reimbursed by Medicare and private insurers. Although this legislation was designed to
stop abusive price hikes, its unintended consequences included limiting price increases even when these may be legitimate such as higher ingredient costs. As a result, the 6% cap on semiannual price increases prevents drug prices from rising with demand, so drug makers cannot cover their costs. Changing the Medicare legislation requires congressional cooperation and action, 2 commodities in short supply in the current political landscape.

**Economic**

- Consolidation within the drug industry: Only about a half-dozen companies make a majority of injectable generics. Some 71% of the market for generic injectables is controlled by the top 3 manufacturers. As mentioned under Regulatory influences, problems that may arise for one producer are typically not compensated by others.
- Generic drugs have slim profit margins: Most of the drugs currently in short supply are older, generic injectables, whose profit margins are razor thin. Manufacturers may not only be loath to enter such a market, but be ready to abandon that market for purely financial reasons, that is, to pursue production of newer, more profitable brand-name products.
- Delays in securing raw materials from suppliers or unanticipated shortages in ingredients.
- Injectable drugs are more complicated and expensive to manufacture, store, and ship than pills. In contrast to generic pills, sterile generic injectables may also require special facilities.
- Just-in-time inventory practices: Although stocking smaller quantities may improve capital efficiency, leaner inventory levels of either raw materials or finished products leave providers less able to withstand shortages.

**Health Care**

- Stockpiling by end-users may exacerbate shortages if providers either hoard drugs or place orders that exceed normal requirements in anticipation of supply problems.
- Changes in clinical practice
- Newly published therapeutic guidelines
- Unanticipated outbreaks of disease

**Are You Experiencing Drug Shortages in Critical Care?**

Because 99.5% of hospitals in the AHA survey reported having one or more drug shortages in the past 6 months, this national problem may exist in your unit. *Critical Care Nurse* is interested in hearing from you on this issue; please take a moment and go to the CCN Web site at www.ccnonline.org, click on the survey link under the cover image to take our survey (by March 31, 2012), and let us know whether and to what extent this national problem has affected your workplace so we can share that information with our readers.

JoAnn Grif Alspach, RN, MSN, EdD
Editor

**References**

12. Life-threatening drug shortages leave patients in limbo. USA Today. October 19, 2011:10A.


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