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Fellows Column: Drug Shortages in the USA is a Persistent Problem

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Introduction:

Drug shortages in the health industry has been a persistent problem for more than a decade in the United States. Drug shortages pose a risk to patients and burden healthcare providers. Since the pandemic hit, drug shortage has followed an increasing trend, and no solution has been found.

The two-year-long COVID pandemic has worsened this shortage of much-needed drugs. Recent news has reported a shortage of Vincristine, a vital drug to treat leukemia, a shortage of Adderall, a commonly-prescribed drug to treat ADHD, and anti-inflammatory tocilizumab used for chemotherapy as well to treat COVID patients. (2) The FDA currently lists 109 drugs in short supply nationally. The American Medical Association calls the shortage an "urgent public health crisis" that "threatens patient care and safety." According to the American Society of Health-System Pharmacists, three of the top five shortages are drugs used for chemotherapy, heart conditions, and antibiotics.

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The effects of the problem, apart from the apparent implication on the patient on such critical diseases like leukemia, ADHD, and COVID, have lots of other side effects such as higher hospital expenses, increasing quality control risks in patient care, and straining the supplies of drugs even more.

Lifesaving drugs:

Some of the lifesaving drugs that are in shortage are the following,

- **Norepinephrine:** used to treat septic shock
- **Bleomycin:** palliative care
- **Lidocaine:** anesthesia
- **Adderall:** Used to treat ADHD

https://www.fda.gov/media/132058/download

Norepinephrine, used to treat septic shock, has had a past shortage. In 2011, the absence of the drug forced physicians to use alternative drugs on patients suffering from septic shock. As a result, the probability of dying from complications was much higher in hospitals that incorporated alternatives than in hospitals using norepinephrine.

Bleomycin is used to treat many forms of cancer, including but not limited to Hodgkin and non-Hodgkin lymphoma. During its shortage in 2016, alternatives to the drug were introduced. Though they were effective, bleomycin alternatives required in-patient care, exposing the patient to pathogens in the facility, increasing stress for loved ones and costs.

Lidocaine, used to reduce burning sensations, is usually associated with propofol, a common anesthetic. When treated with propofol without lidocaine, patients have reported burning sensations, increasing stress, and agitation during a procedure.

Adderall is a drug used to manage attention deficit hyperactive disorder. Patients who do not get this medication can become more disruptive since their symptoms are poorly controlled with other less potent drugs. Adderall is sometimes prescribed as a last resort when the alternatives do not work. (4)

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Impact on public health and economy:

Physicians are forced to decide who receives the needed medication and who does not. There will be delays in getting critical medication or treatment. There is a higher chance of medication errors and accidents when pharmacists have to prepare desired concentrations independently, e.g., preparing pediatric dosing using adult formulations. Physicians are forced to use an alternative drug that may be either less potent or produce more side effects. Treatment duration can be prolonged, resulting in increased costs and health complications.

Possible causes:

There are multiple causes for the problem, some of them longstanding: A NIH commissioned study did a survey and found out that the main reasons were manufacturing problems (23%), supply and demand issues (13%), discontinued drugs (6%) and raw material shortages (3%). However, the same study classified a large percentage (55%) as unknown. A survey by Kesselheim et

al. further illustrated the severity of the drug shortage and concluded that rationing and hoarding were prevalent in large hospitals, further compromising health care. An FDA study concluded that the drug shortage crisis does not follow a typical market response. In a typical market, a shortage results in a price increase addressed by increased supply by existing and new manufacturers to meet the demand. However, the market for prescription drugs, especially generic ones, differs from other markets. The study found three major causes for the shortage: (5)

- Manufacturing drugs with little benefit economics-wise: Due to restricting market circumstances, firms lack the incentive to participate in the market for older prescription drugs. Firms are more interested in profiting from newer drugs, whereas firms that produce older generic drugs are put in a difficult position. (5)
- The economy and drug market give no reward to manufacturers for well-thought-out management systems: The Current Good Manufacturing Practices (CGMPs) regulate the requirements for the production of drugs. The CGMPs, however, only give a bare minimum expectation and not a high standard for mature management systems that guarantee a reliable and high-quality supply of drugs. In order to lower the costs of manufacturing, firms must minimize investment in manufacturing quality, which, in turn, reduces the quality of the product.
- The market cannot come back from regulatory and logistical setbacks: Many companies have their production or contract companies overseas. Due to the complexity involved in the supply chain, response to a drug shortage is not immediate, or it sometimes does not happen due to regulatory challenges. If a new company wants to enter the US drug market and is willing to produce the drug in shortage, the manufacturer has to develop a file and wait for FDA approval, which is a long process. (6)

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Possible Solutions:

Utilizing a long-term solution that ensures a stable, reliable, and sufficient supply of essential medications is essential. Though this problem is significant, the FDA poses three recommendations to combat it.

The first recommendation is to have a system that provides transparency to the solution and brings more awareness of the problem. Research should be conducted to narrow down, isolate, and solve the problem.

The second recommendation is to implement a rating system to incentivize the manufacturers, and the last recommendation is to consider new contracting approaches to ensure a reliable supply of essential drugs. (8) Hospitals must consider including a directory of pharmacies at the hospital in order to have a well-thought-out plan to manage shortages, implement structured communications between distributors to recognize shortages in a timely manner, ask the right questions to find the root cause of the shortage, purchase only from official channels, and have the right amount of inventory. For example, periodic risk assessments should often be conducted to identify manufacturing supply vulnerabilities.

The third solution is to lengthen the expiration date, which can be achieved by increasing the quality of storage and transport. According to the US Food and Drug Administration, expiry dates can be lengthened through manufacturers or the Shelf-Life Extension Program. SLEP extends the shelf life of certain materials after the products go through selective periodic stability testing through the FDA and will minimize product waste.

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Conclusion:

Drug shortages create many challenges for healthcare professionals and patients. Drug shortages significantly impact treatment duration, patient safety, health risks, side effects, quality outcomes, and hospital expenses and costs. Although it is difficult to predict and prepare for every drug shortage, careful planning, and preparation can prevent drug shortage crises and major disasters. Establishing clear procedures and guidelines and timely communications are critical for managing drug shortages at the hospital level.

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