WHY ARE THERE SO MANY DRUG SHORTAGES?

In the past 10 years, an increasing number of drug shortages have resulted in tremendous frustration among practitioners who want only the best treatment for their patients but who cannot always depend that the best drugs for that treatment will be available when needed. Penicillin G, dexamethasone, fentanyl, ketamine, and propofol are only a few that have been back-ordered recently. Why does this occur, and how can it be fixed? Like cancer, the causes are multifactorial, and the cures may be just as elusive.

The propofol shortage resulted from 2 major problems. The first involved an unjust, ridiculous medical-legal verdict involving a major generic drug manufacturer, Teva Pharmaceuticals, which had an estimated 40% of the U.S. marketshare of propofol. The manufacturer announced that they will no longer produce propofol because it is difficult and expensive to manufacture the emulsion, its profit margin is small, and a court ordered it to pay \$356 million to 1 man who was among 144 people to develop hepatitis C from a practitioner who connected the same large, single-use vial of propofol to the IVs of multiple patients. Teva's partner, Baxter International, was ordered to pay \$144 million. Obviously, this outbreak of hepatitis C had absolutely nothing to do with the drug itself, nor with Teva's manufacturing process, packaging, or labeling, but rather with its inappropriate unsanitary use by a practitioner who apparently did not understand or care that every component of an intravenous infusion, including the IV catheter, infusion bag and tubing, and all syringes and needles connected to it, is a single-use disposable item that is considered contaminated once connected to any other component that is connected to the IV catheter in the patient's vein. Thus, if an infusion pump tubing is connected to an IV line, the pump's syringe, tubing, and contents are also considered contaminated for a subsequent patient and cannot be used again. Likewise, if a sterile needle and syringe is used to remove a dose from a multiple-dose vial of drug, subsequent doses must be removed with a different sterile needle and syringe, because the original syringe and needle are immediately considered contaminated once the drug is injected into the IV line and must be discarded rather than being reused to draw up additional doses from a sterile vial. Otherwise, the sterile multiple-dose vial can become contaminated for the next patient's dose.

So, a drug manufacturer's increased medical-legal liability from overzealous prosecution in an ultra-liberal

court system is one cause of drug shortages, because it discourages companies from making or from continuing to make certain drugs with greater liability risk. Do juries actually think that every drug vial, syringe, needle, intravenous catheter, and bag of saline with tubing must have a black box warning tag attached that mandates that the practitioner not use unsanitary techniques? Should the plaintiff's lawyer also have included additional "deep pockets," such as the construction company that built the treatment facility where the drugs were administered, and the city power company that provided the electricity to power the infusion pump? Clearly Teva Pharmaceuticals was unfairly included in the lawsuit because they were considered "deep pockets" to enhance the settlement for the patient and his trial lawyer, even though the drug company did nothing wrong. Although any drug misused in this way could have been involved in the outbreak of hepatitis C, propofol has the added risk of spreading bacterial septicemia when it is used inappropriately, because it can promote bacterial growth when exposed to the environment for longer than the manufacturer warns. With billions of dollars of potential lawsuits from the other 143 hepatitis C victims looming and anticipated increased misuse of propofol by practitioners who are not trained in the administration of general anesthetics, it is a wise business decision not only for Teva to stop making propofol, but also for every other manufacturer to consider doing the same if the court system continues to unjustly hold drug companies responsible for gross misuse of their products.

A second cause of the propofol shortage involved another drug manufacturer that had problems with noncompliance with the FDA's good manufacturing practices and had to halt its production until the situation could be remedied. Problems with other drugs in short supply may be due to use of old-fashioned manufacturing equipment, retirement of key manufacturing personnel, budgetary reallocations of funds from manufacturing maintenance to research or marketing, and manufacturing problems of subcontractors who supply the raw materials. Another cause of drug shortages involves one company buying out its competitors, so that the drug is eventually manufactured by only a single company. If a problem with that single-source company occurs, such as a strike, flood, hurricane, fire, bankruptcy, or FDA closure of a plant for some type of violation, a shortage of that drug suddenly occurs. Any of these factors can result in a temporary or permanent halt in drug production.

The FDA is responsible for helping with drug shortages, particularly if the drug is deemed a "medical ne-

cessity” and has no other reasonable alternative that can be substituted for it. In these special cases, the FDA may assist a manufacturer in fixing its compliance issues or may encourage renewal of its production of a product that may have been voluntarily dropped for financial reasons. The FDA even deemed a non-FDA-approved foreign-made propofol to be a “medical necessity drug” and allowed it to be marketed in the United States at the height of the propofol shortage. However, although the FDA cannot force a manufacturer to make a drug that is in short supply, it can facilitate the approval process for any company that wishes to start making the drug.

How can we survive these drug shortage events? Certainly hoarding a large stockpile of drugs is expensive, and unfortunately hoarded drugs may expire before they can be used. Hoarding of drugs, of course, also precipitates an even more acute shortage once the first rumors of an impending shortage surface. With our typical easy access to wholesale distributors to rapidly replenish our drug supplies whenever needed, many practices use the economical drug reordering principle of “just in time,” similar to the philosophy of maintaining a very low inventory of parts that Japanese automobile manufacturers introduced to their industry. However, the repeated instances of drug shortages in recent years should prompt us to carefully reevaluate our drug purchasing and inventory philosophies. Because one never knows which drug will be the next one to be rationed nor how long the shortage will exist, the wise practitioner should consider having perhaps a 6-month supply of each drug that is considered invaluable to his/her practice. A review

of the year’s previous purchase records could be a reasonable guide to determine how many packages of each critical drug should be the 6-month minimum in stock before reordering. Drugs such as propofol, midazolam, ketamine, fentanyl, remifentanyl, esmolol, ephedrine, epinephrine, phenylephrine, atropine, lidocaine, sevoflurane, dantrolene, and succinylcholine are fairly unique drugs without which I would not want to practice. I would therefore recommend storing a 6-month supply of each of these and carefully rotating the stock so that none of it expires before it can be used. Once the supply of any drug drops below the 6-month inventory minimum, I would reorder. Because there are reasonable alternatives to drugs that I also frequently use, such as dexamethasone, ondansetron, labetalol, diphenhydramine, glycopyrrolate, hydralazine, and metoprolol, for example, I would maintain only a small inventory of them. This practice-preserving inventory philosophy may be a sensible solution to a potential patient care problem over which we have no other control. Although the added inventory ties up additional working capital, the added security to be able to continue to offer anesthesia services of the highest quality and safety for my patients despite drug shortages is well worth the time and effort required to make this change. Our patients deserve the best sedation and anesthesia we can give with the best drugs available in spite of drug shortages.

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