Intro

CB: Welcome back to The Med Thread. Today we've got a special guest with us. Sarah is a recent graduate of Memorial and our pharmacy resident here. She's had an interesting topic in mind for us to chat about, and we're super excited to have her join us. Welcome Sarah!

MC: Thanks for joining us Sarah. Yesterday I went to the mall looking for a new pair of shoes. I get there, look through some of the options and one catches my eye. I've got to try it on though, so I ask the salesperson for my size. They go back to check and come out saying they don't have it. I ask them to check another store, and 10 minutes later, they tell me it's available there and they are willing to ship it over to me. But it'll take 5 business days. So I walk out of the store 20 minutes later with nothing, and I have to come back in a week.

We've all experienced something like this before. But what happens when it's medications?

SW: Drug shortages are becoming an increasingly prevalent conversation topic within the profession. Most health care professionals cringe when they hear the word "drug shortage" or "backorder", and it is certainly a problem that is burdening our health care system.

Today, we will discuss the realities of the drug shortage crisis in Canada. We will dive into a history of how they have affected the health care sector over the past number of years, and why drug shortages happen in the first place. We will discuss how the United States is looking to integrate into Canadian Pharmaceutical Industry, and finally, we will look at how us as health care practitioners can better manage drug shortages in order to provide the least amount of disruption to the workflow and to our patient's care.

Part 1: The current climate

MC: According to Health Canada, a drug shortage can be defined as a situation in which the manufacturer is unable to meet the demand for a drug. This leads to a chain of wholesalers, pharmacies, and ultimately patients being unable to acquire that medication. In 2018, Abacus Data survey indicated that one in four Canadians have been either personally affected or know of someone who has been affected by a drug shortage. For pharmacists, it's an everyday occurrence. We have a story here:
(Abacus survey: https://www.pharmacists.ca/news-events/news/one-in-four-canadians-touched-by-drug-shortage-in-last-3-years/)

CB: One example that I can think of that has been a recent little crisis in the pharmacy world is the nifedipine XL shortage. This is the brand name Adalat XL and there are quite a number of patients on this medication. And when it first went on backorder, I was in community, and I realized, it was just the 30 mg strength that had gone on backorder. So not too hard of a situation, since I could easily call a prescriber and say "if this patient's blood pressure is controlled, maybe they could go to the 20 mg dose." That could be something that they could tolerate and may still get them at the blood pressure target that they're looking for. The other option is that if they're not controlled, to have the opportunity to increase it up to 60. The 20s and the 60s were still available. So unfortunately, that quickly changed, because the supply and demand changes because then with the 30s not available, the 20s went short and then the 60s went short. So then all of the Adalat went short pretty quickly. And I'm not quite sure why the

shortage occurred, but I believe it had something to do with manufacturing, and after switching patients to the 20s, when they went on backorder, we had to switch them to another agent like amlodipine. Or sometimes the physician was smart enough to think that something else might be coming down the pipeline in terms of these drug shortages and switching them to amlodipine right from the get go.

MC: Yes, we had a similar situation working at a community pharmacy. We had an Epival shortage, divalproex. And this one was a little bit harder to switch because a lot of patients will use it for seizure disorders or bipolar disorder and they are well controlled on this medication. So what ended up happening, again, we were not sure the reason for the shortage and we heard that there was a manufacturing issue, but really that doesn't tell us a whole lot. So the pharmacy chain I was working for started rationing out the orders, so each store could not order more than 1 or 2 bottles of the medication per week. That seemed to help weather some of the supply and demand issue, but for patients, it could be quite difficult because some patients take several of these tablets a day and if they don't have it, they get seizures. The other option was to switch them to valproic acid but then that one also came up short, similar to what happened with the nifedipine strengths.

CB: And I know the rationing is certainly frustrating, when it comes to community. But as a pharmacist, when you recognize something is going on backorder, your first reflex is to order as much as you possibly can before it happens. But rationing is certainly the more just way to do things.

MC: Yes, we're thinking about our patients right, the number of patients we have on those medications. We don't want them to be short and sometimes it's hard to think outside of that and realize that this is happening everywhere and if you have a lot in stock, good for your patients, but others are left out to dry.

SW: Many pharmacists have been feeling the burden of drug shortages on their day-to-day work increase within the past few years. As well, increasing presence of media in the profession allows for much more public visibility and commentary around the situation. The outcry surrounding drug shortages has been happening for many years. In 2012, an emergency debate was started in the House of Commons after drug manufacturer Sandoz was forced to discontinue or disrupt production of a large number of products due to quality control issues. This lead to the institution of voluntary reporting of drug shortages by manufacturers, which was then changed to mandatory reporting in 2017 as per Health Canada legislation. *(CD Howe Report: https://www.cdhowe.org/public-policy-research/assessing-canada's-drug-shortage-problem)*

But why is it that drug shortages happen in the first place? There are many factors that can contribute to a shortage, and that can vary depending on if it is a generic drug shortage or brand drug shortage. Generic drug shortages are the most common, as over 70% of shortages occur within generic drugs. Generic drug shortages are often caused by a shortage in one company, which means that the burden of drug production of that medication is split amongst the remaining generic companies in the market. The remaining companies are often not able to adjust their manufacturing schedule or budget to accommodate for this increased demand, and the other companies can also fall into a shortage. This cascade of shortages for a drug can even potentiate to span across drug classes. For instance, the large valsartan recall from this year is showing a chain effect of other angiotensin receptor blockers going on backorder, likely due to patient care teams looking to prescribe alternatives for their patients at a quick rate.

CB: Sometimes, companies can stop production of a drug because it is no longer profitable. This consolidates the market. This can also be seen when companies merge, for example, if company "A" purchases company "B", company "A" may decide that some of the drugs that company "B" produces is no longer profitable and therefore those drugs can be discontinued. This tightens the market. Sometimes, quality control issues can shut down production as the company looks to solve the problem. This was the case with Alysena tablets, a generic form of the oral contraceptive Alesse. These went on backorder due to chipped tablets in some of the packages.

MC: Right, this cascade of shortages happens quite often because the pharmaceutical company has a production facility that is making a certain medication and when they finish making that medication and they have to make something else, they have to go through a long cycle of cleaning the machinery, retesting the machinery, and recalibrating everything before they do this and that may impact their manufacturing schedule.

MC: So a couple of years ago, Tylenol #1, the brand name product decided that they weren't going to manufacture more of their product. So the generic manufacturer had to make up for that demand. Unfortunately for the people who were using the brand name product, they now had no options and they had to switch to something else. But as we eluded to before, if everybody had to switch to something else, it's very likely that there'll be a shortage in that other product as well.

CB: In the same vein, in the last couple month, the brand name Atasol-30 is not being produced as well and that's being switched to other generics and who knows, we might see that go on backorder and have that cascading effect. Another example that comes to mind, is the brand name OxyContin, and how it's formulation was changed to OxyNEO, to make it a more safer product and to be less involved in drug diversion. So actually when the formulation was changed, it was now a much more expensive product and we ran into coverage issues. So patients who were using OxyContin didn't necessarily automatically be able to get OxyNEO. Right now there are generic version of OxyContin that are available, that patients are often taking, so we didn't get very further ahead with a safer product because it came at a much more expensive price tag.

Part 2: A little bit about the USA

SW: Drug manufacturing companies in Canada buy the raw molecular form of the drug they make from Active Pharmaceutical Ingredients manufacturers, or API manufacturers. Many of these companies are located overseas, however are regulated by the Canadian government for good manufacturing practice. Should the factory not meet standards, this may lead to a temporary or permanent shut down of production, which can significantly limit a drug manufacturing company from sourcing the materials they need in order to produce their product. This can affect brand and generic companies alike, as brand drug companies are outsourcing their API production more and more in order to maintain cost-effective production. Often times, all generic companies, or sometimes even the brand name companies for a certain medication may all be sourced from the same API manufacturer, which can cause blanket shortages across all manufacturers in the case of an API company shut down.

Many Canadian drug companies, particularly generic companies, are running on tighter annual budgets as the provincial government puts tighter limits on the maximum costs for popular and medically necessary drugs, in order to limit costs for patients. The lower profit and potentialloss

that generic companies are experiencing may require companies to cut production of lower-performing drugs, or they may be narrowing their predictions of the demand of a drug in order to avoid over-producing and lowering profits, which may lead to a shortage if their predictions are incorrect. As discussions ramp up regarding a potential national pharmacare program in Canada, the potential addition of bulk purchasing for drugs may lead to certain generic companies having a larger share of the market of that drug, and should that manufacturer have a quality control problem at some point down the line it may lead to increased drug shortages.

MC: And we talked about how companies buy other companies, and this is short of the case here. In Canada, we don't have that many generic drug companies, so if one company stops production, then we might be out of the drug completely.

A little different in the US. The US have a lot more generic drug companies. But they have their own set of problems. US senator Bernie Sanders recently made headlines by crossing the Canadian border to purchase insulin, for which he says is about 1/10 the price in Canada as compared to the US. Both Sanders, and current US president Donald Trump, endorse the concept of American residents being able to import necessary medications from Canada, at a fraction of the cost that citizens would pay in the US. Trump defines this as the "Safe Importation Action Plan", which would allow pharmacies and drug manufacturers to submit proposals to import prescriptions from Canada for federal approval. The Canadian Federal Government has maintained an open-minded stance on the topic and have assured that they will put procedures in place to ensure Canadians will not be negatively impacted by this decision.
(US Plan: https://www.hhs.gov/sites/default/files/safe-importation-action-plan.pdf)

CB: American drug prices, particularly for brand name drugs, are significantly higher than that of our country. While the market competition keeps generic drug prices down in the US, the American Federal government is not allowed to negotiate drug prices with manufacturers, and therefore brand name manufacturers have a monopoly on the price of the medications they produce. The Canadian Government, in form of the Patented Medicine Prices Review Board, work together with innovator drug companies to negotiate to ensure that the medication is fairly priced so that unnecessary costs for Canadian patients are limited. The Canadian government compares the prices of proposed medications to those seen in other countries to ensure they are just.

SW: And actually, in a very recent change, the PMPRB, removed the US and Switzerland from the list of reference countries because the prices were just too high. There has been very public backlash from Canadian advocacy organizations about the potential American export of drugs. The Canadian Pharmacist's Association has released a joint statement with the American Pharmacists Association publicly opposing the importation of Canadian Drugs to the US. In this statement they cite concerns of patient safety due to being unable to appropriately assess patient's medical history across borders, as well as concerns about Canadian industry being able to keep up with such a large population increase. The Canadian Medical Association has also publicly opposed this concept, worried about potential increased shortages and that the supply in Canada does not exist to meet this new demand. However, should this change be implemented, the good news is that the Canadian market will have some time to prepare, as these changes will likely take years to implement.
(APhA, CPhA joint statement: https://www.pharmacists.ca/news-events/news/american-and-canadian-pharmacist-associations-warn-that-drug-importation-policies-could-put-patients-at-risk/

News release: https://www.theglobeandmail.com/business/article-us-to-establish-system-for-importing-prescription-drugs-from-canada/)

MC: Some of these policies already exist for drugs that we don't make in Canada. So there are policies that allow pharmacies and physicians to import drugs from other countries for certain conditions where the drug is just not approved in Canada, but that's a very small number of people.

Part 3: What can pharmacists do?

SW: When many of us think about drug shortages, EpiPens are often the first thing to come to mind. EpiPens have gone on backorder many times over the past years. Recently, a lot of us may think about the situation where competitor product Allerject was recalled and all of the patients that were using Allerject were switched to EpiPen as the alternative. This led to a supply and demand issue where EpiPen manufacturers just couldn't keep up with the increased demand. However there are many factors contributing to EpiPen frequently going on backorder. For instance, the expiry on EpiPens is actually quite short, usually about a year. And every September, schools often mandate that their students have two new EpiPens accessible for the school. So the parents are going to pharmacies in September to purchase new EpiPens.

CB: And I know that in community, we're trying to really combat this. And unfortunately, when it goes on backorder, you do have to ration it out, in order for every child to at least have access to one EpiPen. So in some cases, we're actually telling parents, there's a shortage, we're on a rationing plan, so your child can only have 1. And sometimes it doesn't go over well, but when you kind of explain that this could result in a child not having any EpiPen, it usually is pretty well received, and when you can get the EpiPen in, you can give it to more patients.

MC: And of course, one of the biggest problems, is that there's only 1 manufacturer of EpiPen, so until we get more manufacturers, it's going to be hard to keep up with the demand.

SW: Now the big question here is, how can us as pharmacists help patients with drug shortages? In Canada, drug shortages are reported through Health Canada's online reporting database, drugshortagescanada.com. This database allows manufacturers to declare when an anticipated shortage exists, when a confirmed shortage exists, as well as discontinuations of drugs. Pharmacists can help manage drug shortages for their patients by being proactive and keeping an eye on anticipated shortages to help either manage stock accordingly, or to have a discussion with patients that may be affected and prepare them and make changes if necessary. Checking with the manufacturer or the wholesaler to help see when the drug is expected to return to stock can help the pharmacist decide whether the shortage for a patient can be managed by providing a short term supply until the shortage subsides, or if it requires intervention such as changing the drug entirely for a longer-term situation. In provinces where pharmacists have the ability to prescribe or medication manage their patient's prescriptions, pharmacists can look to maximize their scope by substituting their patients prescriptions wherever possible, in order to limit the increasing burden on the health care system caused by referring patients to their physician or the ER for new prescriptions.

CB: And I think this is a great opportunity for professional collaboration when a medication is going on backorder. And if you work with a particular team of physicians, making them aware and suggesting alternatives, and deal with the situation before it ends up being a crisis is always a

great idea. So educating and having a conversation with prescribers about what's the next best choice if the drug looks like it'll go on backorder or is already on backorder.

Conclusion

MC: And we have one more story here where this interprofessional collaboration works quite well. And it's the vitamin K injectable shortage we experienced this past year and experienced before as well. So vitamin K injection is given to newborns to prevent a bleeding disease and it's also used to treat severe bleeding due to warfarin use. So in the hospital, the hospital produced a guide to tell prescribers when they should use oral vitamin K instead of the injectable, to make sure there's enough injectable vitamin K to go around, especially for the newborns and the people that are bleeding out.

CB: And these are all contingency plans. Hospitals, community pharmacies and organizations create these plans in cases of shortages, but we cannot anticipate all of them. And in your day to day patient care, it's quite hard, partly due to incomplete information, distribution problems, and hoarding.

SW: Ultimately, drug shortages are always going to be something that's going to be present in our profession. The best solution is going to be collaboration between patients, the pharmacy team and prescribers, in order to deal with these situations for our patients.

MC: Thanks for listening to this episode of the Med Thread. And thanks so much for joining us Sarah. We hope to have you back in the future for another chat. For our next episode, we'll be joined by our other resident and they'll be talking about what they're interested in.

CB: And as always, you can send any suggestions and comments to medthread@mun.ca. We'd be happy to hear from you! I'll catch you next time!