Episode: *Ethics Talk: Supply Chain Reasons Your Pharmacy Might Not Have Your Medicine*

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[bright, plucky theme music]

[00:00:02] TIM HOFF: Welcome to *Ethics Talk*, the *American Medical Association Journal of Ethics* podcast on ethics in health and health care. I'm your host, Tim Hoff. The most important thing that well organized and well-maintained supply chains deliver to organizations is predictability. In health care, predictability increases reliability of the correspondence between what patients need and what clinicians who care for those patients can deliver in real time. During shortages, and in cases in which supply chains of critical medical supplies, including drugs, are compromised, health care organizations must rely on stockpiles and rationing protocols. Patients who find themselves unable to source medication or unable to afford increased prices resulting from limited supply sometimes also ration their medications. In short, supply chains' vulnerabilities can mean that patients don't get their needs met and that clinicians suffer substantial distress about not being able to care for patients according to how they're trained and according to standards of care.

For health care organizations, functional supply chains are much more than just competitive advantages in the marketplace. Supply chain security and resiliency can be matters of life and death, so their importance is not just clinical or economical, but ethical. International drug supply lines need cooperation and collaboration from drug manufacturers and shipping companies, health care organizations, governments, and policy makers in order to make sure that needed medicines get to clinicians and patients in time and as needed.

Joining us to discuss how critical medical supply chains are identified and secured is Dr Amy Cadwallader, the director of regulatory and public policy development at US Pharmacopeia. Dr Cadwallader also served as the editorial fellow who helped curate this month's issue of the Journal. [music fades] Dr Cadwallader, thank you so much for being on the podcast.

DR AMY CADWALLADER: Thank you, Tim, for having me. It's been a real pleasure to work on this issue and to bring more attention to this really important topic. I'm glad to talk to you today.

[00:02:12] HOFF: A common theme in this month's issue is "essential medicines." And now that's kind of an odd term, because I would imagine most people would consider the medications that they take to be essential. But what this refers to in most cases is the List Of Essential Medicines maintained by the WHO. So, what is this list and the way it's prepared and the way it's updated? Tell us about the particular areas of concern or focus for global health supply chains.

CADWALLADER: That's a great question. Thanks, Tim. So, the World Health Organization does publish an Essential Medicines List and a companion to that, an Essential Medicines List For Children, that are updated every two years. The aims of these WHO lists are to address global health priorities, to identify the medicines that provide the greatest benefits to a population, and to identify which medicines should be available and affordable for everyone. The medicines on the WHO list are selected with regard to disease prevalence around the globe

and public health relevance, among some other factors, and this is really all to satisfy the priority health care needs of a population. The WHO lists also guide the development of individual country-level Essential Medicines Lists, and these country-level lists influence things like national formularies, prescribing and practice guidelines for health care providers, price negotiations, procurement mechanisms, and many other things. And it's important to note that there's considerable variation between the medicines that are included on these lists at the country level.

[00:03:52] How essential medicines are defined and what drugs are included on these lists and the purposes of these lists are really important because they're directly linked to and serve as the impetus for numerous policy efforts/initiatives to improve medicine supply chain resiliency and reliability. And this includes things like investments in innovation, decisions about what to stockpile, trade decisions, and a lot more. And because of the variability, I mentioned the country-level variability, but there's more variability beyond that. And an example of this is there's no common definition of or approach for these lists. Even in the United States we have more than one. The FDA has a List Of Essential Medicines that is intended to make sure that the American public is protected against outbreaks of emerging infectious diseases like COVID-19, as well as other chemical or biological threats that could arise.

The Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response, also known as ASPR, also has a list that was developed that includes prioritized essential medicines that are most critically needed for acute patient care. And this includes things that we think of as acute emergencies like the emergency department or rescue or lifesaving efforts. And there's a third list, even, in the United States that the US Department of Commerce keeps track of. And this includes medicines, but it has a different objective to facilitate ongoing targeted analysis of trade data and information. And while each of these lists has a different objective, there's one thing that they all have in common. It's that they don't necessarily take into account a medicine's risk of shortage or how vulnerable its supply chain is.

[00:06:00] And the definition of essential and critical medicines and the purposes of these lists, if it isn't properly targeted, can leave countries, regions, or parts of the globe unprepared or underprepared if finite resources are misdirected or used elsewhere. With all these factors that I noted, the evaluation of essential and critical medicines really should be based on clinical importance and the demand indicators that we talked about, but also on their supply chain and the vulnerabilities associated with it. And I think that thinking through this and more factors being included into determining essential medicines can result in better outcomes for patients.

[00:06:50] HOFF: So, you mentioned that there's a sort of plurality of lists. There's the list maintained by the FDA. There's the Commerce Department, HHS. What do these lists actually do, for lack of a better way of phrasing this question? Do they compel local health organizations to maintain stockpiles? Do they have some kind of regulatory weight that health departments need to follow? What do they do besides serve as just a point of reference for these organizations?

CADWALLADER: I think that that's a great question, and I also think that that's a topic of a lot of ongoing conversations. The commerce list, for example, really is used when thinking about trade and trade policies. The FDA's list really is targeted at emerging infectious diseases. It has 227 drugs and biological products on it, and many of them are medical countermeasures. The HHS ASPR list really is targeted for that acute care that I said. So, they all have a different purpose. And I think one of the things that's important to note, and that you alluded to when you

asked the question, is that I think everybody has their own definition of what is essential for them. I think that the medicines that I take are essential for me. I'm sure that you would have a similar opinion. So, I think when we're taking a look at these lists that we need to really consider the reason the list was developed and the underlying use and utility that it has. Some of them are used in some conversations when we're talking about regulations and potential legislation, but I don't, to the best of my knowledge, none of them are specifically written into legislation or regulations at this time.

HOFF: Hmm. So, it's not like the FDA adds a medicine to their list, and that means that we need to have X number of doses available at any given time.

CADWALLADER: That's correct.

[00:08:55] HOFF: Hmm. That's very interesting. But speaking of pluralities where we often only see one, we refer to, even in this issue a few times, to the "supply chain." But the reality is that there's innumerable supply chains routing resources back and forth all over the world. It might be obvious that a health care organization, or even a single hospital, would require dozens, if not hundreds, of independent supply chains to provide food and medical equipment, cleaning products, medications, among many other things, to its staff and to its patients. But some people might be surprised by the network of supply chains that support even apparently simple interactions. So, can you give us an example of a seemingly simple operation that requires multiple supply chains that people might not know about and talk a bit about how awareness of this supply chain plurality can help us anticipate problems?

CADWALLADER: Sure. I really love this question, and I'm going to use an example of a pretty basic prescription medicine that I think we've all encountered. Let's take, for example, an oral antibiotic. The supply chains for this pill might at first seem straightforward, that a manufacturer makes this pill, and then that pill is sent to hospitals and pharmacies, patients get it, and we take it. But the full story is really, really much more complicated than that. First, let's break down the basic parts of the product. There's the pill that contains active pharmaceutical ingredient, aka the active part of the medicine that kills the bacteria or whatever we're using it for. There are excipients and binders, and then there's also product packaging to consider. And each of these components likely has multiple associated supply chains. The active pharmaceutical ingredients, for example, require what are called key starting materials, and these are the building blocks that are needed to create the actual ingredient. And each one of these key starting materials has their own supply chain, and often there are several key starting materials that are needed to synthesize just one ingredient.

[00:11:13] And the same scenario is true for excipients and for binders. Each of them has their own key starting materials and related supply chains. And notably, there are sometimes some serious risks associated with some of these excipient supply chains, because some of the components are industrial chemicals that have really complex manufacturing process and come from industries that aren't dedicated to the production of health care products or medicines. And then product packaging is yet another consideration. Product labels, product inserts, bottles, blister packs, all of that have individual supply chains to consider as well.

So, to recap, each key starting material needed to make active ingredients and all the excipients and every other component that is in that pill has a supply chain. Each part of the packaging has a supply chain. And they're all, in general, their own independent supply chains. And if you think about it, what I've described is for one oral antibiotic pill that somebody is taking. If we were talking about an injectable medicine or a medicine that is administered via a device, the supply

chains get significantly more complex and increase in number. And if you add on to that any special handling considerations that some components or drugs require, such as temperature or light sensitivity, the complexity of these supply chains increases yet again.

So, summing up, we can think about the number of supply chains here I noted and multiply that number by the number of medicines that a hospital needs to have in stock at all times, and there's an exponential increase in complexity. And I'll just add that we talked about just medicines and pills here, and we haven't even started to think about other essential items such as personal protective equipment, the food that you talked about, and the cleaning supplies that we need to make sure we have sterile surfaces. So, there's a lot involved in the supply chain in these processes.

HOFF: Hmm. Yeah, the image of all of these complex, intertwined supply chains necessary to deliver something like a single pill to a health care organization is striking. So, thank you for laying that out so clearly.

[00:13:40] Something that's often suggested as a potential solution to some of the problems plaguing overly long or complex supply chains is supply chain segmentation. So, can you tell us a bit about how that works to increase the resilience of supply chains to unexpected problems?

CADWALLADER: Sure. Segmentation as an approach to designing a supply chain that, in the specific case of medical products, can cater to a wide range of products and improve the efficiency of a system. The intent of segmentation is to manage complexities, to increase flexibility and adaptability of the workflows, and to manage some positive and negative tradeoffs. In the case of medical products, segmentation allows for grouping of products with similar product or patient characteristic so that each group can be managed best according to the characteristics that it might require. Some think about segmentation approaches as an alternative to sort of a one-size-fits-all approach for supply chains and use examples like disease-specific supply chains for a specific cancer or cold transport required supply chains for some medicines that require refrigeration.

And the purpose of segmentation is really to develop and implement the right supply chain solutions for different products or patients that are necessary to get the products to them effectively. And under this model, different products are served through different processes, different organizational policies, and different operational modes. And this segmentation strategy can then lead to more sufficient supply chains that operate more effectively and improve the availability of some products, potentially at a lower cost. And it's important to note that there may not be one type of segmentation that will support all medical supply chain decisions in the same way, but rather, there's likely a set of different segmentations that can accommodate the broad scope and breadth that is necessary for diverse patient care.

[00:15:58] HOFF: Yeah, I'm glad you brought up the potential for improved supply chains to lower the cost of goods for an organization. In fact, supply chains operated by for-profit organizations often prioritize efficiency and leanness in their operations. And while this, like you mentioned, in theory, keeps prices in check and ensures a rapid flow of goods, it also leaves supply chains more vulnerable than they might be if they instead emphasized things like redundancy and sustainability. In a recent article, Dr Michael Saunders suggests that a "person-centered approach to supply chain management is needed to help organize health supply chains to be responsive, not primarily to the economic concerns of health care delivery, but to the person at the end of the chain who is receiving the care." So, how might health care

organizations move toward this person-centered model of supply chain health, and in what ways have they done this already?

CADWALLADER: Yeah, thanks for this question. I think that the concept of a person-centered approach to supply chain management is a really great one. One way to start to move in that direction is for more individuals at the point of care—physicians, nurses, pharmacists—really to gain more understanding about the supply chains that are critical for their roles as caregivers. If we start there, and these folks really start to understand the complexity and all that goes into getting each medicine to a patient in need and the processes that are involved to make each N-95 mask needed for protection, there might be more of a willingness to appreciate and demand the resiliency and sustainability that we talk about. I also think that perhaps if individuals leading supply chain logistics had a better understanding of the impact that these medicines and personal protective equipment have in the health care setting for every patient, for every health care provider, that they might view their duty a little bit differently.

[00:17:59] In the article that you mentioned, Dr Saunders talks about the idea of bringing together and integrating health supply chain teams and frontline health care workers. And I really think that this is a great concept and reinforces my initial thoughts about this question. It's really easy for all of us to do our work in a silo and be really good at it, but not necessarily understand or consider the ripple effects. Breaking down those silo walls, I think, is a really good first step. And this journal issue, I think, is a good step in helping to do that in the education process.

[00:18:40] HOFF: You mentioned that it's important for folks at the point of care to have a more thorough understanding of how supply chains work and potential problems, but it's their position in the supply chain, specifically at the end of the supply chain, that makes it difficult to really see those things. They often only see the effects of supply chain logistics when things go wrong, and of course, it's almost invisible when things are going right. So, is there anything that people working at the "end of the chain" can do to help identify problems or build resiliency into supply chains before things go wrong?

CADWALLADER: I think one answer to this is to start to think about, or put a higher value on, the resilience and reliability of supply chains as a standard part of our everyday lives. We all know that lower priced drugs have a higher likelihood of shortage, and the association between the drug price and drug shortages is well documented even by the FDA. And by this, I mean that oftentimes people at the end of the supply chain, as you noted, buyers, patients, for example, are looking for the cheapest version of the products that they're seeking because they have a limited budget to work with or their organizational financial situation to consider when purchasing for a hospital, for example.

And for much of the medical supply chain, this has caused what a lot of folks refer to as a race to the bottom in pricing that has implications for the quality of products, for the resilience of the supply chain, and the supply chain's reliability. And that means that many manufacturers need to price their products low to remain competitive in the market and to legitimately stay in business. Manufacturers that produce the same low priced generic drugs compete predominantly on this price since many of these products are generic and interchangeable. And the resiliency of these drug product supply chains isn't currently highly valued in the marketplace, and sometimes that competitive, because of these competitive prices, they can be lower than the actual cost to produce the product.

[00:20:59] And that result is margins that become very low or even negative for manufacturers. And these lower margins then result in a limited ability to reinvest in the facilities where these products are being manufactured. And everyday maintenance and innovation, manufacturing updates, updates to quality assurance all become really, really difficult. And this also can cause manufacturers to seek lower cost geographies for sourcing and manufacturing. And all of these factors can lead to increased risk of a quality issue or a production line failure. And if those who are purchasing, both for large facilities and at pharmacies and at the drugstore, if we put a higher value on quality and reliability, and we're willing to pay a few cents more for some of these really essential fundamental products, we could potentially improve resiliency. [theme music returns] So, I think really, there's a culture shift and a behavior change that is necessary if we want to move the needle.

[00:22:12] HOFF: Dr Cadwallader, thank you so much for your time on the podcast today, and thanks again for your role as editorial fellow to help curate this issue.

CADWALLADER: Thank you. It's been my pleasure. It's been a really, really great experience working with you and the Journal.

HOFF: That's all for this month's episode. Thanks to Dr Amy Cadwallader for being here, and again, for curating this month's issue of the Journal. Music, as always, was by the Blue Dot Sessions. To read the full issue on *Global Health Supply Chain Security*, head to our site, journalofethics.org. Follow us on social media @journalofethics for all of our latest news and updates. And we'll be back next month with Lloyd Duplechan to discuss *Antimicrobial Resistance*. Talk to you then.