A Painful Reality: Unequal Access to Opioids in Developing Nations

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Vincent, a young medical assistant in rural Ghana, is called away from an interview with myself and other visiting research students to triage a new trauma patient. Minutes later, he returns and reveals to us that the patient was a 35-year-old man with end-stage cancer who was brought to the hospital following a suicide attempt, which was ultimately successful. “He couldn’t tolerate the pain,” Vincent explained. “The temptation to relieve his pain overcame him.” Without access to adequate pain control, which we depend on in developed countries, this young man opted to end his own life as his only remedy.

While the global population continues to age, and with great advancements in the treatment of infectious disease, the burden of cancer and other chronic diseases is rapidly growing worldwide. In Western medicine, palliative care is a subspecialty focused on providing relief from the symptoms and stress of a serious illness. Palliative care services are readily available in developed countries, and these services play a crucial role in both end-of-life care and management of chronic suffering. However, in low-income countries, these professional services are few and far between, leaving millions to live with severe pain without hope for relief. Around two-thirds of patients with advanced cancer have pain. However, only about 6% of all specialty-trained palliative care services are located in Asia and Africa, where the majority of the world’s population lives [1]. Similarly, the developing world only accounts for about 6% of the global morphine consumption, despite being home to almost 80% of the world’s population [2]. In fact, more than 150 countries have no access to morphine [3]. Felecia Knaul, an international health economist and author of a groundbreaking 2017 Lancet publication on this topic, says the disparity in access to palliative pain control across the world is “one of the greatest, most ubiquitous, and at the same time most remediable inequities I’ve ever seen in any area of public health or social development” [4].

An inadequate supply of controlled and prescribed pain treatments has led many African countries to illicitly grow and use cannabis, which is the main drug of abuse, accounting for over 60% of drug treatment demand in the region [4]. Legalizing medicinal cannabis to address the pain treatment disparity is a highly debated topic, but it cannot currently serve as a suitable solution due to the unproven efficacy of cannabis against moderate to severe cancer pain. Increasing the availability of oral opioid formulations and professional palliative care services in these regions would not only reduce the illicit use of cannabis but would also provide a more effective and controlled alternative to treating pain.

High quality cancer treatment facilities and adequate training of cancer specialists may be unattainable in resource-poor areas due to the immense costs and demands for infrastructure. However, it has been shown that palliative care can be a cost-
effective public health entity. Morphine has traditionally been the pain treatment of choice in the developing world. Compared to other opioids and separate drug classes, such as anxiolytics and analgesics, morphine has appropriate strength for treating cancer pain while also having widespread availability, familiarity, and low cost. Quite simply, morphine is effective, easy to make, and amazingly cheap. Ten milligrams of generic morphine should only cost about 1 cent (U.S.) to produce, and a recent report determined that enough morphine to treat the entire world for end-of-life suffering would cost only $145 million a year. This is miniscule compared to the $100 billion a year that the world’s governments spend on enforcing the global prohibition of drug use” [4].

The low cost of morphine makes it the archetypal cost-effective pain relief medications for low- and middle-income countries. However, despite its low production cost, countries face an uneven playing field when it comes to paying for morphine, it has been found that drug companies preferentially supply more expensive opioids to low-income countries; drug companies are uninterested in selling generic morphine because it yields little profit [4]. The overall cost of essential medicines needed to deliver palliative care in Rwanda would cost the country three times more than if the nation had access to the lowest international prices. For injectable morphine alone, Rwanda pays nearly six times the lowest price [4]. The inaction of policymakers worldwide, who are likely influenced by the American opioid epidemic, are allowing big pharma to restrict access of affordable morphine to those who need it most. Allowing the pharmaceutical industry to restrict access of affordable pain medications to low-resource countries is, simply, an abuse of power. With increased awareness and advocacy, policymakers around the world could pass legislation forcing pharmaceutical companies to make oral immediate-
release, off-patent morphine more affordable in order to meet the worldwide demand.

It is clear that the ripples of the American opioid epidemic are being felt around the globe. Because of this epidemic, the word “opioid” has acquired a harshly negative subtext. Legislators and philanthropists in the developing world are now opposing the import of opioids out of fear that increasing availability will trigger another epidemic of addiction abroad. Meg O’Brien, founder of Treat the Pain, a group devoted to bringing palliative care to developing countries, believes this “opiophobia” is illogical. As she stated in a recent interview, “The U.S. also has an obesity epidemic, but no one is proposing that we withhold food aid from South Sudan” [5]. The most recent World Health Organization List of Essential Medicines includes 14 palliative care medications, including morphine and codeine [6]. Therefore, governments restricting opioid imports due to fear of an American-style epidemic is a marked overreaction that fundamentally denies its people medicines that are part of the “minimum medical needs for a basic healthcare system.”

Uganda is a prime example of a nation that has implemented a successful model for innovative palliative care in Africa. Uganda’s success in improving access to opioids has been facilitated by long-standing public-private partnerships between Uganda’s government and private hospice organizations. These agreements have led to the allocation of specific funding for the purchase and local manufacturing of morphine. In addition, orally administered liquid morphine is now locally reconstituted and distributed, free of cost to the patient [7]. Diluting and packaging morphine in drinkable bottles prevents the possibility of intravenous administration, which inherently lowers the abuse potential while appropriately relieving pain. Importantly, this increased access to therapeutic opioids in Uganda without evidence of illicit diversion [9]. Perhaps as important as opioid availability is the broadening of opioid prescribers. This was achieved in Uganda in 2004 with a government-supported statute that permits nurses and clinical officers who have undergone specialized training to legally prescribe oral morphine for pain management [8]. As a result of the collective effort to increase opioid availability for palliative care, morphine consumption increased more than three-fold in Uganda between 2010 and 2014 [7].

The Ugandan model is one that can serve as a blueprint for other Sub-Saharan African countries to follow, but it is not a standalone fix. Despite the increase in availability, opioids are still largely unavailable at public health facilities, are unaffordable as a result of regulations from pharmaceutical companies that limit supply, and are associated with persistent negative attitudes and fear surrounding opioid prescribing [7].

Prevention is generally considered the keystone of public health ideology, but we cannot morally continue to ignore those who are already suffering. Philanthropists and well-intended clinicians cannot solve the problem on their own, and Uganda’s success has demonstrated that improved palliative care is feasible even in resource-poor settings if there is adequate and prioritized government support. As long as policymakers continue to allow pharmaceutical companies to determine who can and cannot access affordable medications, the developing world will not stand a chance. While pain has neither a viral internet challenge to raise awareness nor a celebrity ambassador, layering pain treatment onto any evolving health care system—no matter the disease—is as vital and reachable a goal as any.

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Science

From Sepsis to Pepsis

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Septic shock is a formidable medical problem, with a mortality rate of greater than 20% and the dubious distinction of being the first among all causes of death in intensive care units [1]. Although we understand that septic shock is caused by systemic infection, the molecular mechanisms by which sepsis exerts its effects in totality, including in shock, remain obscure. Therefore, virtually all of the recent clinical trials aimed at reversing septic shock pharmacologically have been unsuccessful. Thus, septic shock remains a condition stubbornly resistant to the miracles of modern medicine, with a considerable risk of death and only supportive treatment available.

He who forgets the past is doomed to repeat it; thus so any discussion of sepsis must begin with a historical perspective on the condition. It was the Egyptians some 4,000 years ago who put forth our first written history of a sepsis-like phenomenon, postulating that a dangerous substance known as “ukhedu” lived in all of our guts and could, if not kept in check, migrate through our blood vessels and even stop our hearts [2]. To stave off this deadly disease, the Egyptians set aside three days each month to give themselves purges and enemas. The Greeks took up the Egyptian concept of ukhedu and generalized it into “sepsis,” which referred to putrefaction and was closely associated with things smelling bad (rotting meat, the contents of the colon). Sepsis was in tight balance with a complementary concept, “pepsi,” which was associated with things smelling good (a delicious pot roast, an aromatic lemon verbena soap).

Having conceptualized sepsis, I will not linger much longer on the historical basis of our modern day understanding. However, a few highlights are too good to ignore, including a 1718 sketch of the “animalcules” that were initially proposed to cause sepsis (Figure 1), a sketch of an early experiment to determine the method of transmission of these animalcules that involved the incubation of various animals in a sealed barrel with putrid material (“miasma”) at its base (Figure 2), and this description of an 1872 study of the bloodborne transmission of putrid material: “Casimir Davaine [a French physician who also discovered anthrax] injected pu-