

Editorial

Opioid Availability in Latin America as a Global Problem: A New Strategy with Regional and National Effects

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Most *Innovations* readers already know that in some countries opioids are not available, and some may even feel that opioids are not sufficiently available in their own work settings. But few probably are aware of the background problems and how these affect the general population in the developing regions of the world, namely Latin America, Africa, Eastern Europe, and Asia. In this edition of *Innovations* we will explain some of the reasons for these problems and present a new model to improve availability of opioids to patients in pain.

Cancer and other conditions that result in acute or chronic pain are frequent and have been increasing.¹ In developed countries, approximately 50 percent of those diagnosed with cancer die of advanced disease, while in developing countries this figure reaches 70 percent.² Pain is one of the most common symptoms in cancer patients and has been estimated to affect between 30 to 40 percent of all cancer patients undergoing treatment and 70 to 90 percent of those with advanced cancer.³

The World Health Organization (WHO) List of Essential Drugs includes drugs that are crucial to treat the most common problems and have proven to be safe, effective, of high quality, and low cost. Opioids, such as codeine, morphine, and pethidine, are included in this list as essential analgesics. In recent years, there has been recognition of the need to improve the availability of opioid medications for the treatment of pain, especially cancer pain.^{4,7}

Each year approximately 2,400 cancer patients per every million inhabitants in a given region suffer pain requiring potent opioids.^{8,9} However, in many developing countries, including those in Latin America, opioids are not always available.

This issue of *Innovations* features a new approach, a model developed by David Joranson, MSSW, director of the Pain and Policy Studies Group (PPSG) at the University of Wisconsin, in Madison. This model for an initiative designed to improve adequate access to opioid analgesics is based on the fact that many governments, through their national laws and regulations, place improper restrictions on the medical use of opioids, in their efforts to prevent drug diversion. The model uses two important strategies: a workshop where regulators and physicians are brought together to discuss their perspectives, obligations, and points of view; and the use of a set of guidelines, in the development of which Mr. Joranson was also centrally involved.

Mr. Joranson has had extensive experience in the field of policy and regulations, first working as a regulator for the state government in Wisconsin, and afterward as an advocate of the concept of "balance" for controlled substances. I have worked with him in several projects, starting in the early 1990s when he gave me technical support and guidance in my effort to obtain morphine for a palliative care program in Cali, Colombia. I also worked with him when I was a fellow of the Pain Research Group, and then in my role as the advisor for the Pan American Health Organization (PAHO), the WHO regional office for the Americas. His efforts in several regions of the world have resulted in better understanding of the laws and regulations, and in several cases, improved access to pain medications.

Also in this issue is a Personal Reflection by Maria Cristina Chirolla, who worked as a regulator for Colombia for several years and participated in the first workshop based on this model, in Quito, Ecuador. Ms. Chirolla reflects on her background as a regulator in a country severely affected by the "war on drugs" and mainly focused on preventing diversion and illicit manufacture. But most importantly, she describes the effect that the workshop and the use of the guidelines had on her personal views, which led her to initiate a program of national scope to improve the availability to opioids for pain relief.

Historical Overview

Many health care professionals are unaware of the international treaties that bind countries of the United Nations and place controls on substances that have a potential for abuse (called "controlled substances"). These treaties also set standards for national laws and affect the prescription, distribution, dispensing, and manufacture of these substances. The international treaties are a result of many events, starting with the Opium Wars in China during the 19th century.

During the 1800s, the United Kingdom of Great Britain, Ireland, and other Colonies waged the Opium Wars on China so as to allow the continuation of the opium trade. The wars led to the legalization of opium importation, and allowed for the free flow of opium from British India into China. The spread of opium smoking created a demand which was unmet with the imported amounts. To meet the demand, poppy cultivation and opium production were drastically increased in China and an estimated 30 million Chinese became opium addicts.¹⁰ At the beginning of the 1900s, it was thought that drug abuse was a local problem for each country, but it became evident that China was unable to handle this enormous drug abuse problem without the cooperation of the countries producing and manufacturing drugs (British India and Britain). This recognition led to the first form of international cooperation in the field of drug control between China and Britain. In 1914, the British Government obliged manufacturers to request a certificate ensuring that the drugs were needed for medical and scientific purposes, thereby controlling all sales and trade. This system failed as a control mechanism; opium was illegally smuggled into China from India and other parts of Asia. The failure of this "bilateral" approach led to the development of multilateral, international treaties and the recognition that this was not a national problem, but an international one, affecting all countries. The International Opium Convention held in Shanghai in 1909 was the consequence of the first international conference on narcotic drugs, which became known as the International Opium Commission. This conference laid the foundation of the current international drug control system.¹⁰

International Treaties

International drug control treaties seek to achieve a balance between the need for narcotic drugs and psychotropic substances for medical and scientific purposes, and the need to prevent their abuse or misuse.¹¹ All member countries of the United Nations are to abide by the treaties. Countries are, however, free to adopt laws and regulations that their governments deem necessary to comply with the international conventions, and to prevent, control, and penalize narcotics abuse, diversion, and illicit trade or manufacture.

The International Narcotics Control Board (INCB) was created by one of these international treaties (the Single Convention on Narcotic Drugs) in order to "limit the cultivation, production, manufacture, and use of drugs to an adequate amount required for medical and scientific purposes, ensure their availability for such purposes and prevent illicit cultivation, production, and manufacture of, and illicit traffic in and use of drugs."¹² In carrying out its responsibilities, the INCB is expected to cooperate with governments and maintain a continuing dialogue with them to meet the aims of the treaties. The INCB calls for a flexible humanitarian approach that aims at ensuring the availability of controlled substances for medical purposes, especially in developing countries, where resources for public health are limited, and has requested national governments to identify barriers in their legislation that interfere with the medical access to morphine and other opioid analgesics.

The INCB serves as the quasi-judicial control organ for the implementation of the United Nations Drug Conventions¹³ and is independent of governments as well as of the United Nations. It is the entity responsible for approving and/or setting each nation's annual production and consumption quotas of substances controlled by the treaties, including potent pain relievers such as morphine. Each year, all countries are required to send to the INCB the estimated amount of opioid medications they will require to fulfill their medical needs. If a country fails to submit the quota before the June deadline, the INCB establishes a quota for that country based on past consumption and trends. Countries are under an obligation not to exceed these amounts, but a country is entitled to ask for an additional amount if the previously set one proves insufficient to satisfy its medical needs.

INCB Annual Reports

The international drug control treaties require the INCB to prepare an annual report on its activities. The report provides a survey of the drug situation in various parts of the world, as well as data on estimated needs, legitimate requirements, production, manufacture, trade, and consumption of controlled substances. The annual reports are supplemented by detailed technical reports that contain data on the licit movement of narcotic drugs and psychotropic substances required for medical and scientific purposes, together with the INCB's analysis of those data. The data are made available to the general public through the INCB's website at www.incb.org/e/ind_tr.htm.

ⁱ The production or manufacture of such drugs and substances as well as their distribution and use, must take place in accordance with control measures designed to achieve the objectives of the Single Convention of Narcotic Drugs of 1954, the Convention on Psychotropic Substances of 1971, and the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances. Copies of these Conventions can be found at www.incb.org/e/ind_tr.htm.

Although the Single Convention on Narcotic Drugs¹² states in its preamble the importance of opioids in relieving pain and suffering, no specific reference is made to cancer pain in this document. However, in recent years, the INCB has realized the important role that opioids play in the treatment of cancer pain, and has stressed this in specific documents that ask governments to make opioids available for pain relief.¹⁴

Steps in the Opioid Availability Process

The steps required to provide opioids to a patient with severe pain include the following:¹⁵

1. The importer applies to its local regulatory authority for an Import Certificate.
2. The importer's regulatory authority (local government agencies responsible for opioid regulation) considers whether the importer is properly licensed and whether the drug and amount are within the country's estimated needs for the drug; if approved, an Import Certificate and one copy are issued to the importer.
3. The importer sends the original certificate to the exporter.
4. The exporter applies to its own local drug regulatory authority for an Export Certificate.
5. The exporter's regulatory authority considers whether an Import Certificate has been issued, and whether the exporter is properly licensed; if approved, an Export Certificate is issued to the exporter.
6. The exporter's regulatory authority sends a copy of the Export Certificate to the importer's regulator authority.
7. The exporter ships the drugs to the importer, along with the originals of the Export Certificate and the Import Certificate.
8. The shipment must successfully pass a customs inspection.
9. After the shipment is received in a given country, the importer must provide both certificates to its regulatory authority and the drugs are manufactured and/or distributed in the country to the retail level (pharmacies and institutions).
10. The patient receives the medication after a licensed physician has prescribed it.
11. The regulatory authorities must provide the information on the amounts of opioids consumed to the INCB.

Additionally, many countries also use a certification process to prevent marketing of pharmaceutical products that are counterfeited, falsely labeled, or do not meet quality standards. If any of these steps are not completed nor taken appropriately, the patient will not receive the medication when needed, or may not have access to it at all.

Several differences exist among countries with mature pain initiatives and those where pain relief is limited. When countries are starting to develop new pain and palliative care programs, barriers at the macro level (such as storage, certificates, licensing, manufacturing, and distribution requirements) become evident. If in the meantime, new programs develop, professionals train, patients become aware of the benefits of the drugs, and the barriers at the macro level are eliminated, end-user barriers, such as limitations to the amounts prescribed and the number of days for treatment, fear of addiction, and issues with cost, come to the fore. In order to have a system that works, barriers need to be dealt with at all these levels. There is very little benefit to patients if limitations to prescription are eliminated, but the institutions and pharmacies are not allowed to store and dispense the drugs, or vice versa.

In countries such as the United States, United Kingdom, and Canada, many legal or regulatory barriers have been eliminated or are being revised. However, issues of cost, lack of education of regulators, physicians, and nurses, or the fear of addiction are still preventing many patients from receiving adequate treatment for pain in these countries.

Trends in Consumption of Opioid Analgesics

The WHO uses morphine consumption data as a broad indicator of progress to improve cancer pain relief, and the INCB collects and reports the consumption data yearly from government reports.

Data from the PPSG and the INCB shows that the consumption of morphine in Latin America is less than 1 percent of all the quantities consumed in the world.^{16,17} and very low compared to countries from North America. Table 1 summarizes morphine utilization in several Latin American countries as expressed in Daily Defined Doses (DDD). DDDs represent the number of daily doses of 30 mgs per million inhabitants based on average consumption reports of the previous five years. The DDD is dose adjusted to 30 mg per day, which, in cases of severe pain, may not be appropriate. Therefore, the DDD is useful as a comparative tool but not as a measure of adequate pain treatment. Another useful comparative tool, which poses fewer problems, is mg per capita. Figure 1 (from David Joranson's Featured Innovation), graphs per capita consumption of morphine in 2000 and offers an alternate way of measuring consumption, which leads to a similar picture of wide disparities in consumption between developed and developing nations.

There are differences in consumption between developed and developing nations, and also among developed ones. Canada, for example, has a higher consumption of morphine than the United States. Among the reasons for this may be that physicians in the United States may be prescribing other potent analgesics and less morphine than those in Canada.

Unavailability of Opioid Medications

The WHO and INCB and other authors have indicated that opioid analgesics are insufficiently available, particularly in developing countries.¹⁸ By requiring a special registration procedure, prescription of morphine and other potent opioids is restricted to a small percentage of physicians. In many countries, opioid use is prohibited or restricted by national laws, by limiting the dosages, concentrations, or the duration of therapy, regardless of the patients' needs.¹⁹ Canadian and US laws

do not impose limits on the duration of treatment or the amount prescribed. Rather, these are determined by the physician, based on the clinical condition of the patient and the pharmacologic characteristics of the drugs. In contrast, a comparative study among several Latin American countries demonstrated that many have adopted overly restrictive laws and regulations, which affect the medical and scientific use of opioids by imposing limits on the dosage and/or the number of days allowed for therapy.¹⁹

The use of opioid medications in developing countries is also significantly affected by cost. Opioid costs in developing countries have been reported to be higher than those in developed nations, and many finished opioid products and commercial preparations for the treatment of pain are either not available or only at very high prices, making them inaccessible to the majority of the population. A comparative study demonstrated that opioids are not only more expensive in absolute dollar value in developing countries, but also as a percentage of the monthly income per capita.²⁰ In Argentina and Mexico, for example, the monthly cost of opioid therapy can be more than 200 percent of the average monthly income. Some possible explanations include:

1. Many developed countries have either socialized medicine or subsidize to some degree the costs of medications. In these countries, patients pay lower prices than the real costs of the drug. The opposite tends to be true in developing countries, where patients are charged higher overheads to cover the costs associated with making those medications available, as well as to generate profit for producers, manufacturers, distributors, and pharmacists.
2. When importing finished products, the costs of import taxes, red tape, and licensing may increase the prices.
3. Distribution channels are less developed and not as sophisticated as in developed countries. Sending out medication from major distribution centers to smaller cities may be a complicated and expensive process.
4. In developing countries with smaller markets and less demand for opioids, the price may be higher in order to cover the costs of production, distribution, and marketing the drugs. On the other hand, larger markets with high demand provide the benefits of economies of scale whereby these costs are spread out through the higher volumes of products.
5. Regulatory and legal restrictions imposed on the distribution, storage, and sale of opioids require that pharmaceutical companies and pharmacies incur additional expenses to comply with those requirements, which may be passed on to the consumer of the medication.

Although the supply of narcotic drugs for medical purposes remains inadequate in many countries, the morphine consumption trends recorded by INCB indicate improvement. The global consumption of morphine has been doubling every five years since 1984, but the trend is due mainly to increasing consumption in developed countries.¹⁸

Strategies to promote opioid use for pain control in Latin America

PAHO recently adopted a Palliative Care Program for the Region. This program includes several projects that promote the availability of opioids, including the workshop for regulators featured in

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this issue of *Innovations*. As mentioned earlier, the workshop design is based on the premise that in order to improve access and availability of opioids, it is important to improve communication among health care professionals and regulators.

In addition to creating the workshop, Mr. Joranson convened a group of individuals under the auspices of the Medications Division in WHO, to create a set of guidelines to help health care professionals and regulators identify barriers to the adequate use of opioids.²¹ He describes this process in some detail in the Featured Innovation of this issue. These guidelines have already been distributed and used widely in Latin America, Asia, and Africa, through similar workshops carried out by the PPSG and endorsed by WHO and its corresponding regional offices.

Two workshops in which the guidelines were used have taken place in Latin America. One workshop was held in December 2000 for countries in the Andean Region (Bolivia, Chile, Colombia, Ecuador, Peru, and Venezuela) and one in July 2002 for Southern Cone countries (Argentina, Brazil, Paraguay, and Uruguay). In both cases, it was observed that in those countries where there is close communication among regulators and health care professionals (e.g., Argentina, Colombia, Chile, and Brazil), palliative care tends to be more developed and there are fewer problems with opioid availability.^{22,23} A workshop for regulators and health care providers in Central America and the Caribbean is projected for 2003. Some of the lasting outcomes of the workshops have been a National Pain Relief Program for Colombia, the elimination of a 24-hour prescription limit for physicians in Peru, and the creation of a National Palliative Care program in Uruguay. Several meetings with leaders in palliative care, policy makers, and regulators at the local level also have taken place and others are planned for the future. In addition, the newly founded Latin American Palliative Care Association has held additional workshops and presentations with policy makers and health care professionals.

Conclusion

There are still many problems regarding adequate availability and access to potent analgesics in Latin American countries. As a result, other initiatives have taken place, such as the PAHO Demonstration Projects, where seven sites with guaranteed access to opioid medication were selected to serve as models of care and training. Other educational initiatives by the PPSG and more recently, the International Association for Hospice and Palliative Care (IAHPC), also hope to play a significant role in making appropriate pain treatment available and accessible.

The Latin American region is still challenged by poverty, lack of education and training, and barriers at the regulatory, legal, and administrative levels. Governments are concerned with such problems as lack of infrastructure and difficulty gaining access to care centers, improving control of acute infections, and vaccinations, and many have yet to place opioid availability on their priority list.

Insofar as improving access to opioids is an international effort, we are all affected to some degree by the decisions and actions taken by others. We need to become aware that opioid availability is not just a local issue, but rather one with no borders. All stakeholders in this process, including patients, professionals, multilateral organizations, the pharmaceutical industry, policy makers, and health care professionals, need to be included in the development of strategies to improve this situation.

The measure of control that these Conventions prescribe varies from one group to another. Drugs are listed in various schedules according to the differences in their dependence producing properties, their therapeutic value and their risk of abuse.

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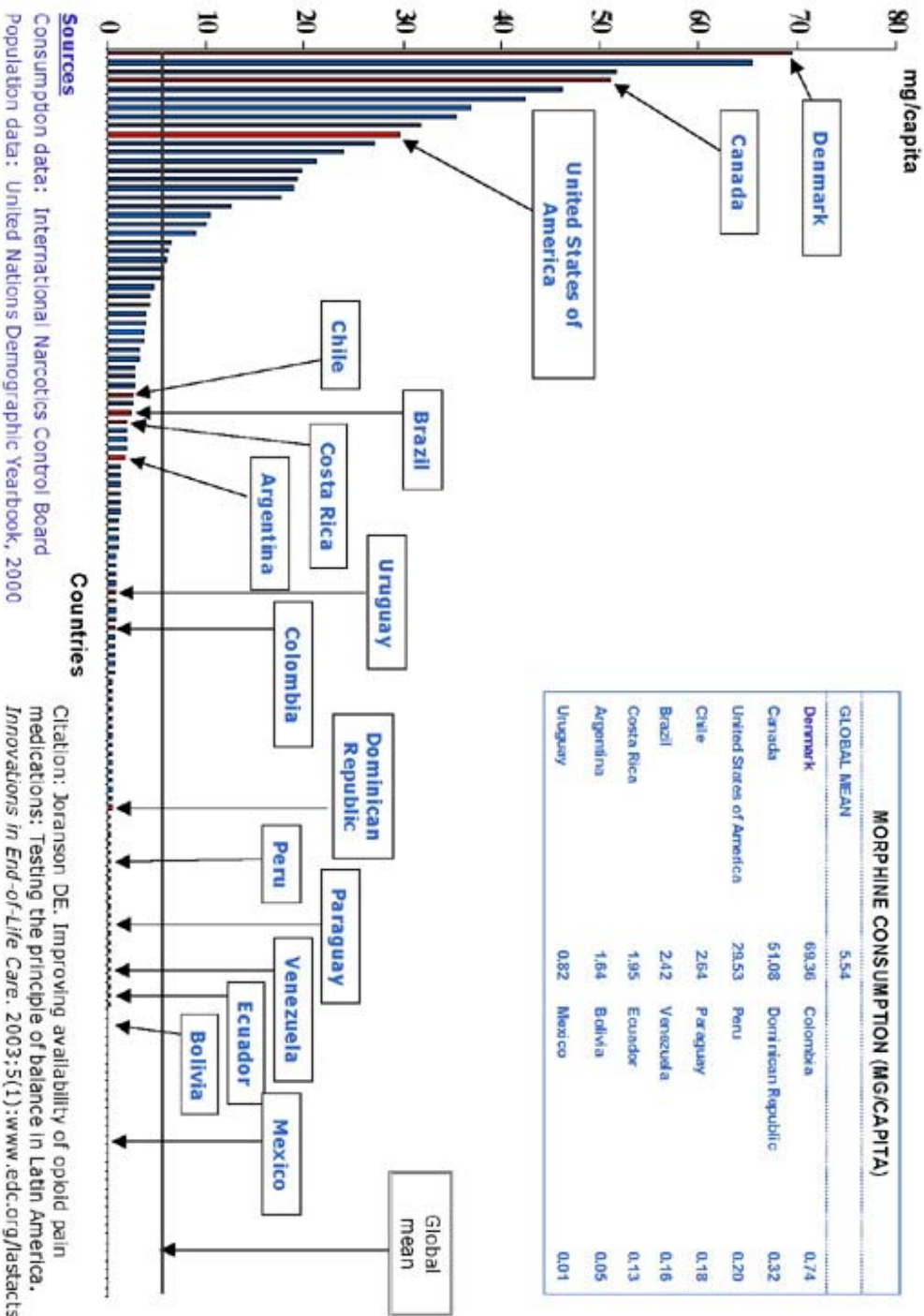
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Table 1:
Average Morphine Consumption in Daily Defined Doses (DDD) for 1996-2000

Country	Average DDD
Argentina	404
Bolivia	2
Brazil	168
Canada	4,130
Chile	174
Colombia	92
Costa Rica	238
Cuba	113
Ecuador	6
Guatemala	2
Honduras	1
Mexico	9
Paraguay	14
Peru	14
Dominican Republic	33
Uruguay	110
USA	2,650
Venezuela	7

DDDs represent the number of daily doses of 30 mg of morphine per million inhabitants based on average consumption reports over the previous five years. Data excerpted from larger chart: International Narcotics Control Board. *Narcotic Drugs: Estimated World Requirements for 2002—Statistics for 2000*. http://www.incb.org/e/ind_tr.htm

Figure 1: Global Per Capita Consumption of Morphine, 2000



Sources
 Consumption data: International Narcotics Control Board
 Population data: United Nations Demographic Yearbook, 2000

Countries
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