An Introduction to Environmental Pharmacology

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First Edition

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Chapter 5

Accumulation and Disposal of Leftover Medications A Key Aspect of PharmEcovigilance

Christian G Daughton & Ilene S Ruhoy

In the introductory overview (chapter 1), we present a conceptual overview of *pharmEcovigilance*. In addition to the traditional focus for pharmacovigilance — adverse effects (or absence of intended effects) in humans and domestic animals caused by appropriate use of medications — an additional objective incorporated in pharmEcovigilance would be to minimize the ecological footprint of medications. A formal approach to pharmEcovigilance would also begin to focus attention on a little-recognized dimension of healthcare — one that could be termed the *healthcare footprint* of medications. Just as an ecological footprint is a multidimensional measure of the impact of actions or activities on the environment, the *healthcare footprint* could be viewed as the overall impact on healthcare by medications. The major objective of pharmEcovigilance would be to minimize the ecological footprint of medications while optimizing their healthcare footprint.

The conceptual diagram in Figure 1 of the overview (see chapter 1 of the same authors) presents the role that pharmacovigilance currently plays in monitoring post-market safety of medications. Also shown are those additional, little-discussed aspects of the post-market "afterlife" of medications that can impact the ecological environment and which should also fall within the purview of pharmacovigilance. PharmEcovigilance, as we have conceptualized it, aligns traditional pharmacovigilance with the added dimension of the ecological environment.

In this paper, we focus on one of the aspects of pharmEcovigilance that has been receiving growing attention, especially in the U.S. — the accumulation and disposal of unwanted, leftover medications. The magnitude of drug stockpiling and accumulation, and eventual disposal of leftover drugs by consumers serves as a multidimensional

measure of the effectiveness of pharmEcovigilance — the greater the magnitude and extent, the less its effectiveness; accumulation and disposal of drugs would indicate failure of a pharmEcovigilance program. It can also serve as a surrogate measure of the efficiency and efficacy of healthcare, and is a major factor in the healthcare footprint. Wastage of medications not only maximizes the ability of active pharmaceutical ingredients (APIs) to enter the environment (with largely unknown consequences), it also directly reflect an inefficient aspect of administration of healthcare, possible non-optimal therapeutic outcomes, and the likelihood that drugs can be diverted to others for unintended purposes (leading to drug abuse and accidental poisonings).

Drug accumulation and disposal are the two key aspects of the life-cycle of drugs that can provide information essential for corrective actions in improving health care and protecting the environment. The data that can be mined from the types and quantities of leftover drugs unused and disposed by consumers can be used to optimize the administration of health care and reduce the incidence of drug abuse and poisonings, while also reducing the possibility of adverse impact of drugs on the environment.

Probably more so than for any other non-food item consumed by humans, pharmaceuticals are used and stored at a broad array of locations throughout society — wherever people live, work, play, or visit. These products are frequently purchased in excess or are not fully consumed as directed (for example, because of patient non-compliance, physician-altered treatment, intolerable effects), leading to the widespread accumulation of unwanted, leftover drugs. Spanning the spectrum of sources such as healthcare facilities, ubiquitous household medicine cabinets, and first aid kits, to less recognized sources such as zoos and cruise ships, there are many locations at which drugs are used and can accumulate, eventually leading to the need for disposal. These sources have been cataloged and discussed by Ruhoy and Daughton (in preparation, 2008); one particular source, never before discussed, has been identified — coroner investigations can yield a wealth of valuable information regarding leftover drugs (Ruhoy and Daughton, 2007).

The relative significance or contribution of each of these sources with respect to disposal is currently unknown. Despite the fact that the accumulation of unused, unwanted, expired medications has long occurred, extremely little is known regarding the identities and amounts of these medications, the portions that become indefinitely stockpiled, or the portions that are subsequently disposed. For those medications that are disposed as waste by consumers, the amounts and types that are disposed by the major routes (namely, flushing to sewer drains or placing in domestic trash/garbage) are also unknown. Because of the differences in the ways that different countries and locales handle drug disposal, broad generalizations are probably not possible. The only general perspective that can be provided is that the types and relative quantities of individual medications used in different countries can differ dramatically (because approved drugs can differ and because prescribing practices and geographic demands can differ), the mechanisms available for disposal of leftover drugs vary, and the way in which a drug is disposed is often dictated by the type of packaging and the acute toxicity of the drug or its propensity for abuse.

The accumulation and disposal of leftover medications is a multidimensional problem. Most of the aspects (see Table 1) are amenable to control measures that could be designed and incorporated into pharmEcovigilance programs.

A major unanswered question concerning drug disposal is whether it has any measurable or significant impact with respect to the occurrence of APIs in the environment (Daughton 2008; Ruhoy and Daughton 2007). Does disposal contribute significantly to the overall quantities of APIs in the environment or to the quantities of particular APIs. Two major aspects of uncertainty exist. First, it is unknown what percentage of any particular API in the environment originates from disposal; the individual percentages probably vary dramatically among individual APIs. Second, disposal undoubtedly occurs from a variety of largely uncharacterized and diverse sources. Sources of disposal, along with the types and quantities of APIs resulting from each source, are important to understand so that effective and efficient pollution prevention approaches can be designed and implemented.

In the U.S., the total lack of drug disposal data that can be derived from well-defined sectors of the general population has only allowed conjectures regarding the significance or environmental impact of drug disposal. With a newly described approach using the inventories of drugs disposed in the course of coroner investigations, Ruhoy and Daughton (2007) have now provided the first means to begin acquiring accurate and representative data on drug disposal so that calculations can be made to assess or predict the overall contribution to environmental pollution by APIs, at least for a particular locale during a specified time period. Equally important, these same data hold the potential to provide important insights into the efficiency and efficacy of healthcare.

While the discussions to date regarding drug accumulation and disposal have dwelled on the contribution of the disposal of API pollutants and on the best approaches for environmentally prudent disposal, comparatively little attention has been placed on understanding why leftover drugs accumulate to begin with. The proper disposal of drugs is important not only for reducing the unnecessary entry of drugs to the environment (such as by flushing or disposal to trash), but perhaps even more so for reducing the problem of human (and animal) morbidity and mortality due to diversion of drugs from accumulated stockpiles awaiting disposal and leading to consequent poisonings and abuse. Indeed, the growing problems with diversion and drug abuse fostered the first U.S. government guidance for consumer disposal of unused drugs, which was issued in February of 2007 by the White House Office of National Drug Control Policy (http://www.whitehousedrugpolicy.gov/drugfact/factsht/proper_disposal.html); the same concerns regarding diversion have led the Substance Abuse and Mental Health Services Administration (SAMHSA) to test a national public education campaign in the US, where consumers receive messages from their pharmacists reminding them to properly dispose of unused prescription drugs (http://www.samhsa.gov/rxsafety/).

Numerous factors control and drive the consumption, accumulation, and disposal of leftover pharmaceuticals by consumers. Most serve to increase use, although several are at work to reduce use (refer Table

1; chapter 1 of this book by Daughton and Ruhoy). Significantly, the influence of most of these factors on the consumer could be reduced or eliminated by various control measures. Accumulation and disposal of drugs can lead to, or contribute to, a number of adverse outcomes. The accumulation of leftover, unwanted drugs can be used as an indicator of three major conditions: (1) Leftover drugs, when disposed to sewage or trash represent a diverse source of potential chemical stressors in the environment (the APIs possess a measurable ecological footprint). (2) Leftover drugs represent wasted healthcare resources and lost opportunities for medical treatment (they increase the healthcare footprint). (3) Accumulated drugs represent increased potential for drug diversion (consumption by those for whom the medication was never intended), which, in turn, can facilitate accidental poisonings and improper or abusive usage; note that while drug abuse is a major problem, the abuse of drugs that are no longer being used by the patient for whom they were prescribed is a problem that occurs partly (or largely) because of the lack of prudent disposal options.

It is clear that a large, diverse array of data can be mined from cataloging leftover, unused, unwanted drugs. These data can then be used to design measures to reduce drug wastage. With reduced wastage, the ecological footprint of medications could be reduced. At the same time, collateral benefits derive from reduced wastage, serving to optimize the healthcare footprint. With drug wastage data, a wide spectrum of weaknesses and liabilities associated with the administration of health care could be revealed and actions taken for improvement.

The magnitude and extent of accumulation and disposal can be used as a measure of overall success of pharmEcovigilance programs (Table 2). A major objective of a pharmEcovigilance program should be to continually lower the incidence of leftover drug accumulation — with an ultimate goal of eliminating the occurrence of leftover drugs. There are numerous routes by which progress could be made (refer Table 1; chapter 1 of this book by Daughton and Ruhoy). Most could be accomplished by changing the human and healthcare processes, activities, and behaviors that lead to accumulation in the first place.

Table 2. Accumulation and Disposal of Medications: Multidimensional Measures of pharmEcovigilance Effectiveness

Indicator	Adverse outcome	Examples
Leftover drugs can indicate:	Medical therapy was never completed	Patient non compliance
	The medication was the incorrect choice for treatment	Ineffective, non-efficacious
	Healthcare resources have been wasted	Money spent on unneeded drugs
	Imprudent consumer behaviour	Hoarding or stockpiling of drugs for possible future use
Accumulatation of drugs can lead to or promote	Diversion to others, resulting in drug abuse or purposeful human poisonings	Addiction and suicide
	Accidental poisonings in humans and pets because of unsecured stockpiling	Infants, toddlers, the elderly, and pets can all inadvertently ingest leftover drugs that become accessible because of unsecured, unattended stockpiling
Disposal of leftover drugs:	Maximizes the introduction of APIs to the environment by by-passing natural ADME processes that ordinarily might have reduced their amounts	In the absence of ADME processes, 100% of each API can be discharged to the environment via disposal by trash or sewage; disposal also increases the need to landfill or incinerate hazardous waste
	Can lead to wildlife poisonings	When discarded unsecured to trash, wildlife scavengers can ingest discarded medications

Summary:

A wide spectrum of forces underlie the generation of leftover drugs, ranging from certain practices of manufacturers, distributors, prescribers, and dispensers, to patients themselves. Much of the need for drug disposal could be eliminated by focusing corrective actions on these forces. If new approaches to medical care were developed that could minimize or eliminate leftover drugs, the consequent environmental residues of APIs would be eliminated, therapeutic outcomes might improve, health care expenses could go down, and human morbidity and mortality (due to addictive usage and poisonings from diverted, leftover drugs) would decline. Reducing, minimizing, or eliminating leftover drugs via an active pharmEcovigilance program represents a very significant opportunity to improve both ecological and human health.

Notice

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