The after-life of drugs: a responsible care initiative for reducing their environmental impact

Best-practice training and protocols in drug disposal should form part of a pact between the health and water sectors

Peter M J Fisher
BSc(Hons), PhD,
Adjunct Professor,
Environment and Planning[1]

David A Smith
BSc,
Manager Product Quality[2]

Peter J Collignon
MB BS(Hons), BSc(Med),
Director of Infectious
Diseases and Microbiology,[3]
and Professor[4]

1 School of Global Studies, Social Science and Planning, RMIT University, Melbourne, VIC.
2 South East Water Ltd, Melbourne, VIC.
3 Canberra Hospital, Canberra, ACT.
4 Medical School, Australian National University, Canberra, ACT.

peter.fisher2@rmit.edu.au

doi: 10.5694/mja12.10904

Few give much thought, if any, to the fate of medications and other chemicals that pass though the bodies of people and animals or are washed from their skins. The conventional wisdom is that the residual amounts of these substances are so minuscule that they are of little or no consequence. That penicillin was recovered from the urine of World War II soldiers was telling evidence that antibiotics, at least, do not just vanish. Even the discovery in 1976 that fish downstream from a Kansas sewerage plant were malformed as a result of exposure to the oestrogen, oestrone, related to contraceptive pill use, failed to change the mindset that the environmental burden of drugs was insignificant.[1]

Two decades then passed before German scientists, looking for herbicides in waterways, stumbled across a chemical they did not recognise.[2] It was the cholesterol-lowering agent clofibrate, a close chemical relative of the weed killer 2,4-D. They investigated further and found analgesics (ibuprofen, diclofenac), antibiotics, lipid regulators (phenazone, fenofibrate), antiseptics, β-blockers, oestradiol, anticonvulsants and x-ray contrast agents. Similar cocktails were subsequently found in the waterways of the United States.[3]

Mixtures of chemicals from human activity are always present in the environment. It is commonly assumed that individual chemicals do not interact. However, a study of the impact of pesticides on Californian frogs[4] highlighted that we have little understanding of synergistic effects between chemicals and of how chemical cocktails behave, because most toxicological studies evaluate individual compounds.

Medicinal watch

The environment can be an important factor in the development and spread of antibiotic-resistant bacteria. Nearly all the genes that encode for resistance have been present in microorganisms for millions of years. We, however, continue to add millions of tonnes of antibiotics, as well as huge numbers of resistant bacteria and their genes, to the environment. These antibiotics and resistant bacteria persist in water and soil. People acquire resistant bacteria from the environment through food and water, especially in developing countries.[5]

The US Environmental Protection Agency (EPA) maintains a watch on steroidal (including sex) hormones (biogenics, pharmaceuticals and steroids) and human drugs.[6] In new water pollution rules, the European Community has recently added three drugs, including the popular pain-reliever diclofenac, to its list for monitoring and control in surface waters.[7]

Compounds with very high environmental persistence of a year or more (eg, cyclophosphamide, diethylstilboestrol and tetracycline) have been identified previously.[8] Other drugs such as fluoroquinolones (eg, ciprofloxacin) will persist for many months (Box).

Drugs with high level of persistence in the environment[8]

Persistence	Drugs
More than 1 year	amitriptyline, clofibrate, codeine, cyclophosphamide, diethylstilboestrol, dextropropoxyphene, erythromycin, ifosfamide, mebrobamate, methyldopa, metronidazole, naproxen, pentobarbitone, sulfadimidine, sulfamethoxazole, sulfasalazine, tetracycline, tolbutamide
More than 1 month	ciprofloxacin

Making sense of the sewerage system

Doctors and health professionals need to be aware of what health care activities put into the sewerage and waste disposal systems. This is particularly important because there is a limited extent to which these systems can deal with the large number of drugs that are stable. Many do biodegrade, but others can be very persistent in their new setting.[9]

The number of compounds not (or only partially) degraded to recalcitrant metabolites (those resistant to biodegradation) in a treatment process depends on the technology used. Conventional wastewater treatment plants can and do break down or remove some of these compounds,[10] but the overall quality of plant performance varies. A glance at annual reports on utility websites is informative in this regard. This variability in performance arises from differences in design and standards of expertise, and (significantly) differences in state EPA regulations. For example, in Sydney, the EPA permits the discharge of primary settled sewage, while in Queensland, there are very tight limits on parameters like nutrient reduction.

The most common treatment process for urban sewage in the developed world is the activated sludge process (ASP). It is capable of producing relatively high-clarity, low-nutrient water when managed correctly. ASP has been shown to remove more than 50% of certain chemicals.[11] Other research has shown varying removal rates for synthetic chemicals, and some drugs are shown to be poorly removed by conventional treatment plants.[12] As the use of recycled water increases, the quality of this water becomes more critical and good management of all sewer inputs by utilities becomes more important. Pharmaceuticals are being identified as a potential risk in recycled water risk-management systems of utilities such as South East Water in Melbourne, Australia, and Orange County Sanitation District in California in the US. This is leading to increased awareness of the waste contributions from domestic catchments and high-concentration point sources such as hospitals.

Treatment plants are the last barrier to the entry of synthesised chemicals to soil systems and waterways. Removal of chemicals at modern plants can be highly efficient, but there are many older, less effective plants. Even higher quality plants do not remove all chemicals foreign to life forms (xenobiotics). In any case, treating this problem at the source ("beginning of pipe") is likely to be much cheaper and more effective than "end of pipe" solutions.

The ability of modern sewage plants to strip pharmaceuticals remains a work in progress. The inherent complexity is underscored by the fact that bacteria, normally friendly workhorses in sewage treatment, can also produce toxic breakdown products. An example is bacteria converting the non-steroidal anti-inflammatory drug (S)-naproxen to (R)-naproxen, which is highly toxic to the liver.[13]

When water is intended to be recycled, there is an added need for drugs to be removed. However, advanced processes such as microfiltration, ultrafiltration, ultraviolet radiation and ozonation are designed more for removing pathogens than for breaking down molecules. These processes are regulated by national guidelines and so tend to be of a similar standard around the country. Treatment involving combinations of reverse osmosis, advanced oxidation, ozonation and activated carbon are the preferred (but expensive) option if the removal of xenobiotics is a priority.

How can the health sector help?

Preventing, or at least minimising, the quantities of more toxic and persistent compounds that enter sewage is a fundamental complement to upgrading treatment plants. Thus, health care professionals should be aware of the need for pharmaceuticals to be managed as organic and persistent pollutants.

Hospitals and clinics constitute point sources of such pollutants, whereas patients in the community are diffuse sources, which are much harder to monitor and manage. While hospitals are hot spots, they are the source of only a modest proportion of all drugs used in people and animals that subsequently enter the environment. However, in the first instance, tackling hot spots in source control could make significant inroads on the drug load entering treatment plants — for example, as much as 25% of all human antibiotics are estimated to be administered in hospitals.[14]

Where waste disposal via sinks is unavoidable, xenobiotic waste streams should be treated before release to the sewer. Indeed, a treatment process at the source may be preferable to facing increased trade waste charges by utilities if they deem hospital wastewater inputs to be problematic. Emptying the contents of half-empty syringes into wash basins (a likely common practice despite protocols to the contrary) should also be discouraged. Rubbish disposal systems that minimise medicines ending up in landfill are another area requiring attention, as sewage treatment plants regularly receive tankers containing leached material from rubbish tips.

> "there is unmet need to train health professionals in how to decrease the environmental burden of medicines"

Health sector reform to reduce the environmental burden of health care has five elements:

- better housekeeping (and training), including discouraging emptying syringes and chemicals like x-ray developing solutions into sinks;[14]
- choosing less toxic, less environmentally persistent, but equally efficacious drugs where possible;
- decreasing overall drug use in the community (where up to 50% of antibiotics taken by people may have limited clinical value[14]);
- establishing protocols to prevent or reduce the release of drugs into the environment, with particular focus on drugs known to be highly toxic and persistent (eg, cytotoxic drugs[14]); and
- exploiting the potential of non-pharmacological approaches to treating pain and depression, and lifestyle measures to tackle prevalent conditions like hypertension and diabetes to reduce the need for pharmaceutical use.

Patients in the community

A good source-control management system leads back to households. An audit of discharges here could provide a profile of the type and quantity of sewered drugs, as well as other products, such as personal care products and sunscreens containing nanosilver particles. Significant advances in detection and analysis make this easier.

Additionally, community awareness programs on drug disposal, such as California's "No drugs down the drain" campaign, should be part of a national initiative to reduce pharmaceutical pollution in water supplies.

What can others do?

Finally, a greater awareness and selectivity by "big pharma" and regulators of the fate of medicines in the environment is needed and, where a less persistent drug will do, its use should be encouraged. Equally, manufacturers should attempt to design future pharmaceuticals to be degraded into harmless components before leaving the sewage treatment plant. The use of drugs with long half-lives that are not readily biodegradable should be discouraged.

The way forward

Australia can build on its reputation for innovation in water management with a responsible care partnership between the health and water sectors. The silent partner in such an arrangement is the pharmaceutical industry, which needs to improve the (bio)degradability of its products. Further, there is unmet need to train health professionals in how to decrease the environmental burden of medicines; this could be extended to the introduction of a specialist subject in academic programs.

The water industry's contribution would be to ensure that their treatment plants are operating under optimal conditions and that the older ones are either replaced or upgraded. Where appropriate, it would also help hospitals with in-house xenobiotic waste treatment.

Competing interests: No relevant disclosures.

Provenance: Not commissioned; externally peer reviewed.

1 Hignite C, Azarnoff DL. Drugs and drug metabolites as environmental contaminants: chlorophenoxyisobutyrate and salicylic acid in sewage water effluent. *Life Sci* 1977; 20: 337-341.

2 Heberer T, Stan HJ. Determination of clofibric acid and N-(phenylsulfonyl)-sarcosine in sewage, river and drinking water. *Int J Environ Anal Chem* 1997; 67: 113-124.

3 Kolpin DW, Furlong ET, Meyer MT, et al. Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999-2000: a national reconnaissance. *Environ Sci Technol* 2002; 36: 1202-1211.

4 Hayes TB, Case P, Chui S, et al. Pesticide mixtures, endocrine disruption, and amphibian declines: are we underestimating the impact? *Environ Health Perspect* 2006; 114 Suppl 1: 40-50.

5 Finley RL, Collignon P, Larsson DG, et al. The scourge of antibiotic resistance: the important role of the environment. *Clin Infect Dis* 2013; May 30. [Epub ahead of print.] doi: 10.1093/cid/cit355.

6 Daughton CG. Environmental stewardship and drugs as pollutants. *Lancet* 2002; 360: 1035-1036.

7 Directive 2013/39/EU of the European Parliament and of the Council of August 12 2013 amending directive 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. (Text with EEA relevance.) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:226:0001:0017:EN:PDF (accessed Sep 2013).

8 Zucato E, Bagnati R, Fioretti F, et al. Environmental loads and detection of pharmaceuticals in Italy. In: Kümmerer K, editor. Pharmaceuticals in the environment: sources, fate, effects and risks. Berlin: Springer, 2001: 19-27.

9 Watkinson AJ, Murby EJ, Costanzo SD. Removal of antibiotics in conventional and advanced wastewater treatment: implications for environmental discharge and wastewater recycling. *Water Res* 2007; 41: 4164-4176.

10 Jelic A, Fatone F, Di Fabio S, et al. Tracing pharmaceuticals in a municipal plant for integrated wastewater and organic solid waste treatment. *Sci Total Environ* 2012; 433: 352-361.

11 Martin Ruel S, Choubert JM, Budzinski H, et al. Occurrence and fate of relevant substances in wastewater treatment plants regarding Water Framework Directive and future legislations. *Water Sci Technol* 2012; 65: 1179-1189.

12 Tan BL, Hawker DW, Müller JF, et al. Modelling of the fate of selected endocrine disruptors in a municipal wastewater treatment plant in South East Queensland, Australia. *Chemosphere* 2007; 69: 644-654.

13 Hashim NH, Nghiem LD, Stuetz RM, Khan SJ. Enantiospecific fate of ibuprofen, ketoprofen and naproxen in a laboratory-scale membrane bioreactor. *Water Res* 2011; 45: 6249-6258.

14 Kümmerer K, editor. Pharmaceuticals in the environment: sources, fate, effects and risks. Berlin: Springer, 2001.