Medicines in the drinking water supply

Mum: wastewater treatment plants are supposed to get rid of all the nasty stuff in sewage, but do they remove everything?

Photo by Gustavo Fring: https://www.pexels.com/photo/mother-giving-pills-to-her-daughter-lying-in-bed-5934472/

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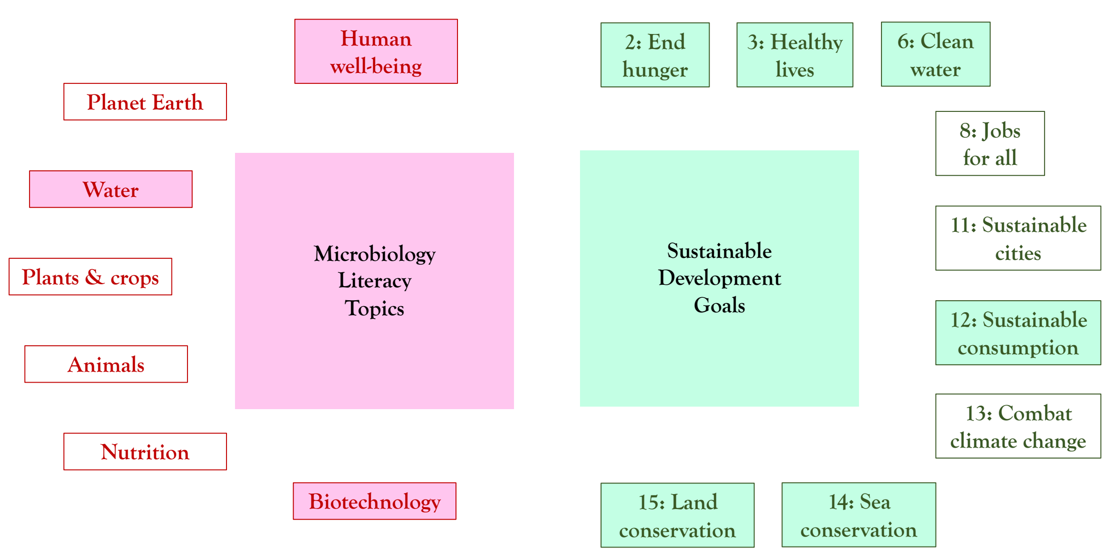
Storyline

Pharmaceutical drugs have a tremendous effect on the well-being of humans. Through them, people can enjoy a better, more active and longer life. At the same time, however, many pharmaceuticals are not readily biodegradable in the wastewater treatment process. They leave traces in the wastewater and, dependent on the process, also in our drinking water. When wastewater treatment plants were conceived and designed over 100 years ago, nobody knew about trace pollutants and the environmental impacts of industrial chemicals and pharmaceutical compounds. Also, many pharmaceuticals are prescribed to ease the symptoms of widespread diseases (i.e. high blood pressure), while often their obvious causes (i.e. lifestyle, nutrition choices, lack of physical exercise) are not considered in therapy. Seriously educating the population about the effects of their eating and exercise habits, and rewarding a healthier lifestyle might, in the long run, be a healthier and more cost-efficient choice for national economies, health services and the environment.

The Microbiology and Societal Context

The microbiology: micropollutants; wastewater treatment; biodegradation; biological recalcitrance; ecotoxicology; antimicrobial resistance; non-target effects of pharmaceuticals. *Sustainability issues:* food production; health; clean water; environmental pollution.

Box 1 – Microbiology theme and SDGs treated in this chapter



Medicines in the drinking water supply: the Microbiology

1. Pharmaceuticals are used to keep people healthy. Pharmaceutical drugs comprise numerous molecules, such as antibiotics, pain killers, steroids and other chemicals commonly used to cure, treat or prevent diseases and maintain our physical and mental performance. Since pharmaceuticals are highly biologically-active chemicals used to target the cause of a specific disease, their improper administration may lead to no effect at best, to side effects in other cases, and especially to metabolic perturbation in non-target organisms.

Nowadays the availability of pharmaceuticals is taken for granted or - even worse – being misused. Commonly, e.g. antibiotics are prescribed and taken even without verification of the presence of an infection which requires treatment, but rather as a preventive measure. This behavior is irresponsible in several ways. Unnecessary self-medication involves taking the chance of being exposed to side effects without any health benefits. Moreover, it can be harmful for the ecosystem, as pharmaceuticals end up polluting our water cycles. Also, in the case of antibiotics, there are risks especially for the future patients that rely on effective treatments, as each time bacteria are exposed to antibiotics, there are chances that they become resistant, and worse yet, share the instructions how to become resistant (i.e. pieces of DNA encoding the resistance genes) with their fellow bacteria.

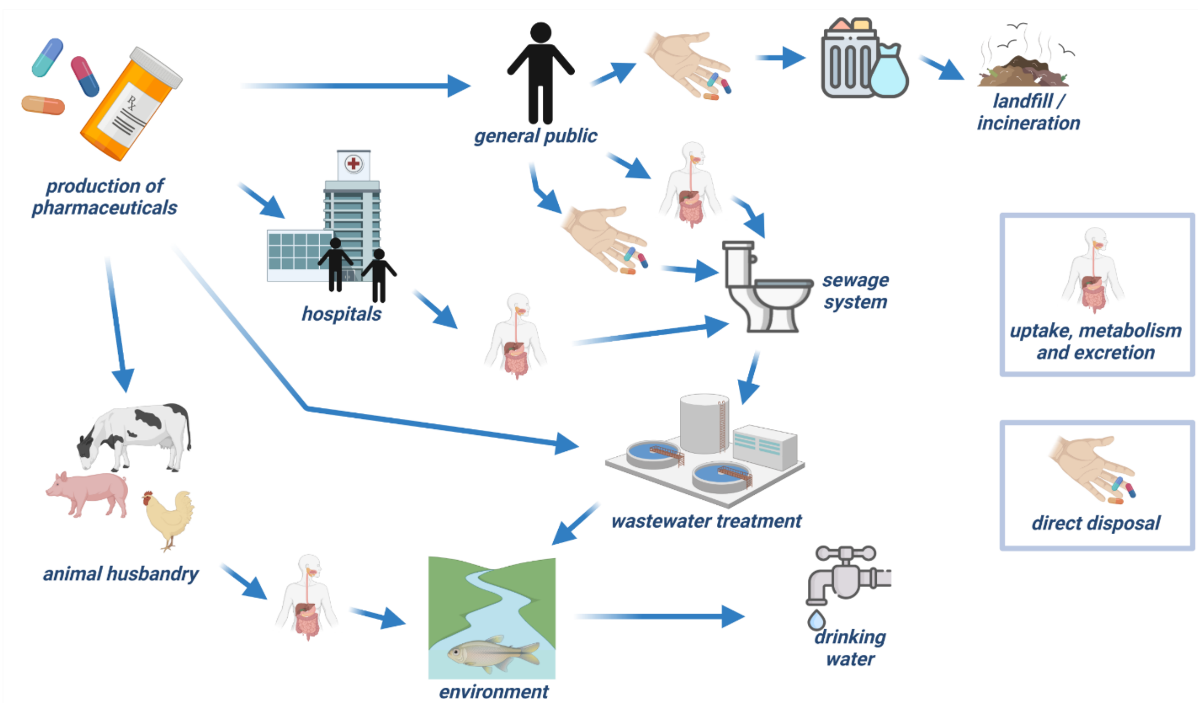
It is important to always remember that pharmaceuticals are outstanding weapons applied and mostly designed by humans to keep people and animals healthy, and not that we are healthy only because we take pharmaceuticals.

2. How they end up in the wastewater treatment system.

A wastewater treatment plant viewed from above (Pixabay).

Pharmaceuticals end up in wastewaters by multiple routes, as indicated in the figure below. Their wrongful disposal inevitably plays an important role in determining their fate. Indeed, the improper disposal of the drugs from the manufacturing plants or via the municipal waste cycle represents the first paths that those chemicals may undertake. Throwing pills, tablets or any other medicines into the toilet (or generally in a non-specific waste container), regardless of their expiration date, is a direct route for them to enter the environment. Moreover, the municipal sewage collects human excretions which contain often unaltered or only slightly modified pharmaceuticals we have taken because we need them. Hospitals especially are considered hotspots releasing bioactive molecules through the sewage system, as the amount of pharmaceuticals per person is particularly high.

The concentration of pharmaceuticals generally found in the environment, regardless the origin, is in the range of few ng L^{-1} to tens of $\mu g\ L^{-1}$. Local concentrations depend, of course, on how these chemicals spread to and within surface and groundwaters. However, even if these concentrations can be quite low, pharmaceuticals are per definition substances characterised by high biological activities that can in some cases exert adverse effects at very low doses, particularly when exposure times are long term (chronic).



The path of the pharmaceuticals from the pill to the drinking water. The pharmaceuticals used in veterinary medicine and in husbandry may directly reach the environment through the animal excretions. The wastewater treatment plants (WWTPs) accommodate effluents containing active principles and their residuals coming from several source including the urban and the hospitals wastewaters. Given the high variability of the compounds that might be present in the receiving waters, the WWTPs cannot remove all of them and this may result in the release into the environment of these chemicals with the biological effect maintained.

3. Consumption, (slight) modification in the body, excretion. Most of the pharmaceuticals typically administrated nowadays are not fully metabolised by the human body. Indeed, part of these chemicals can be excreted unaltered and reach wastewater treatment plants through the sewage system. Most wastewater treatment plants are not designed to remove such contaminants. Hence, these compounds can pass unchanged into the environment and consequently be found in the water cycle, and even our drinking water.

Some pharmaceuticals can be totally or partially metabolised by the body. This can result in the release of different metabolites into the environment. These can be further modified through microbial processes within the water cycle. In some cases, such metabolites can exhibit a similar or even increased toxicity compared to the original (parent) pharmaceutical.

4. The goal of wastewater treatment is to prevent harmful substances entering the environment. As previously mentioned, wastewater treatment plants are not usually designed to effectively remove or fully degrade all the possible pharmaceuticals (or their transformation products). However, these treatment plants are the key players in the water cycle for physical, chemical and biological removal of contaminants in wastewater and the sewage system, before release of treated water into the environment.

The main treatment step for removal of organic pollutants, i.e. the biological treatment step, requires microbes which feed on organic matter, thus removing it from the water. Hence, wastewater gets mixed with microbes, often in form of a sludge, to digest pollutants. However, there are different kinds of pollutants. Some of these are easily biodegradable, present in high concentrations (in the range of few to few hundred mg L^{-1}), and are degraded quickly and almost completely. Others are hardly degraded because they are not readily biodegradable and often only present in very low concentrations (few ng L^{-1}), two factors that render biodegradation difficult and sometimes even very unlikely.

After the biological removal of the pollutants the effluents are treated, e.g. by sedimentation, to remove the majority of the microorganisms and to pass the cleaned water into the environment.

5. Biodegradation in the wastewater treatment plants. Biological processes within wastewater treatments remove compounds which are potentially harmful for humans and the environment. These processes rely on microorganisms. The microbial community present, e.g. in sludge, can degrade – effectively: use as food – a multitude of compounds, including certain pharmaceuticals, but also other man-made products, generally called xenobiotics. In general, the biodiversity, i.e. the multitude of different species, present in the biological treatment step also reflects its potential to degrade certain substances. Therefore, consortia of microorganisms are essential to provide the biological digestive capability of the treatment plants.

On a molecular level, biodegradation depends on enzymes present in the members of the community. These enzymes usually catalyse the degradation or the production of "natural" compounds of the cell. However, often the chemical structures of some xenobiotics, or at least part of the structures, are similar to those of their natural counterparts, so the enzymes can degrade them, too. Yet the bacteria do not decide what they consume, as they cannot differentiate their actual food from these foreign substances. As a result, they may occasionally transform certain pollutants to compounds that may be harmful (to them and sometimes to us).

In many cases, when xenobiotics are regularly present in sufficient quantities in wastewater to represent a reliable food source, microbes can over time evolve new metabolic capabilities so that they become able to efficiently degrade xenobiotics and use them as food to gain energy and grow. This, of course, is also driven by the advantage they gain by specialising on substances other microbes are not using.

Yet there is a high diversity of chemicals entering the wastewater treatment cycle and this fortuitous degradation does not apply to all xenobiotics. Therefore, many substances are not degraded or only modified in a way that they may still negatively impact on the environment. So, after passing through the wastewater treatment process mainly unchanged, they are released into the receiving streams.

Some substances may also stick to the sludge flocs. On one hand, this is good, as they are removed from the water cycle. On the other hand, in many countries, sludge from the wastewater treatment process is used as a fertilizer in agriculture as it contains important nutrients, such as phosphorus. However, application of the sludge onto fields facilitates the release into the environment of the chemicals sticking to it. This is a serious drawback of an otherwise great opportunity to recycle the sludge to avoid its discharge in landfills or incineration.

6. Why biodegradation does not always work so well, especially with many man-made chemicals and trace compounds. The term biodegradation generally refers to the transformation of a chemical structure of a compound to another with different chemical properties. However, the fact that a substance has been biodegraded according to this definition does not imply anything about whether it is still harmful or not.

Over the ages, microbes have developed many ways to degrade the organic matter present and abundant in nature, such sugars, lipids or proteins, including organic matter produced by organisms as waste. These biomolecules are mainly composed of carbon, oxygen, hydrogen and nitrogen. In most cases, microbes can efficiently degrade such compounds and thereby acquire both the energy and carbon needed to metabolise and grow. In general, the majority of carbon-based compounds are biodegradable.

However, although certain man-made chemicals (e.g. pharmaceuticals) exhibit similar chemical structures to those of natural compounds, their biodegradation often does not proceed as expected. Specific chemical substituents or even the complexity of the molecular structure itself can render man-made substances more difficult to degrade. Radiocontrast agents, typically used in nuclear medicine (radiology), is one typical example how the presence of certain elements (halogens, specifically iodine), dramatically decreases their degradability, as microorganisms are not usually equipped to deal with these substituents.

But the potential degradability of pharmaceuticals (or xenobiotics more generally) in the environment also depends on the corresponding concentrations. Pharmaceuticals are mainly found in wastewater treatment plants, and even later in the water cycle, at concentrations between low ng L^{-1} to low μg L^{-1}. Enzymes are far more inefficient at degrading potential substrates present in low concentrations than in saturating concentrations, so compounds present in concentrations of a few ng L^{-1} are degraded at extremely low rates. Moreover, if pharmaceuticals are only present in very low concentrations at which there is no need for detoxification or at which they are not attractive as a food source, the evolution of improved degradation capacity will have no selective advantage and hence there will be no evolutionary driving force to develop new or better ways of degradation.

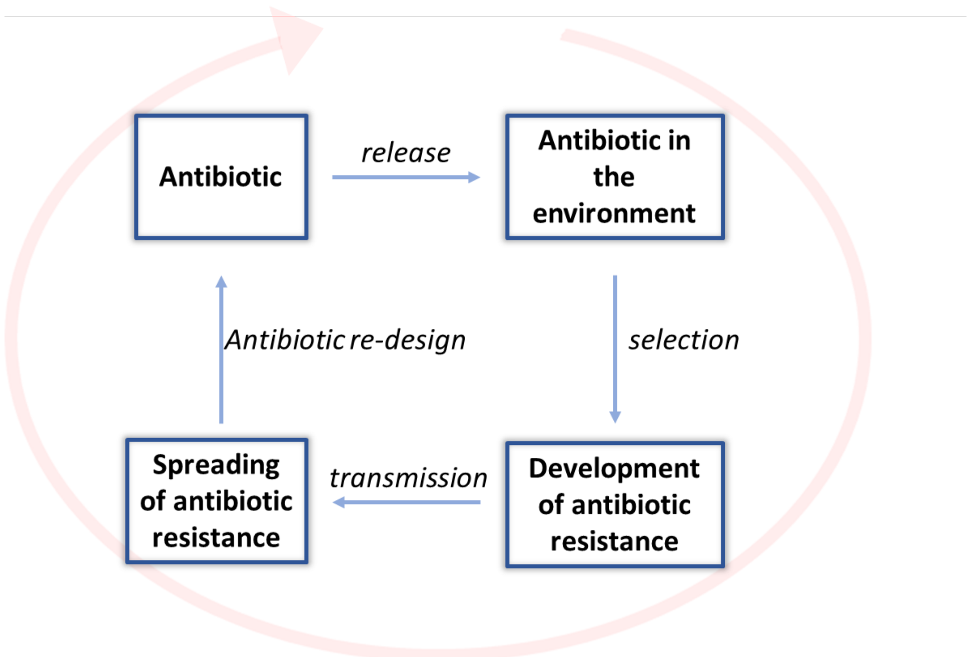
7. The problem of pharmaceuticals in the environment. Today, humanity cannot abandon the massive use of pharmaceuticals and its demand will even increase. With improving economic welfare, more people will be able to afford necessary medication. Furthermore, the world population will continue to grow and there is a global aging process of society. One of the reasons for the increasing frequency of detection of pharmaceuticals in the environment is the advancing technology enabling lower detection limits and more consistent results analysing soil or water samples. Yet the abundance of these compounds in the environment epitomizes the price of the technological progress that has been made since the last century.

One of the major concerns regarding the constant release of these chemicals is the lack of a proper discharge system starting right at an urban level, as well as a proper awareness of citizens. Given the really high number of compounds released into water bodies or soils, it is not easy to generally outline the environmental consequences that such releases may cause. However, many of these chemicals represent a potential risk for both the ecosystem and the health of living beings. Only a better and exhaustive comprehension of their environmental fate will help the design effective strategies to remove and prevent release of emerging pollutants into the ecosystem. “Emerging pollutant” refers to compounds for which the removal shall be necessary, given their potential negative impact. However, no official guidelines are currently available and their effects in the environment are not well defined.

8. Antibiotics, antibiotic resistances and an imminent demand for more antibiotics. Antibiotics are substances that kill or slow down or inhibit the growth of bacteria and other microbes that cause infections. However, antibiotics are powerful selective agents for the evolution and aquisition of antibiotic resistance in antibiotic-exposed microbes. The release of antibiotics into the environment is inevitably connected to the emergence of new antibiotic resistance genes (ARGs) in the microbes naturally present in these ecosystems. As stated above, the concentrations at which you can find these compounds are in the order of magnitude of ng L^{-1} to µg L^{-1} which is far below minimal concentrations inhibitory or fatal for microbes. Yet sub-inhibitory concentrations of antibiotic can still be stressful and a selective force for the evolution and dissemination of antibiotic resistance.

There are multiple routes for dissemination of resistances. An important one is horizontal gene transfer or HGT, in which resistant cells transmit the genetic information encoding their resistance determinants to sensitive cells (it is quite common for bacteria to exchange bits and pieces of useful genetic information with others in a microbial community). Another is vertical gene transfer, where the trait of antibiotic resistance is transferred to the offspring of resistant bacteria. In addition to the transfer mechanisms, passive resistance may occur when cells able to inactivate the antimicrobial agent protect neighbouring susceptible cells.

Since the antibiotics released into the environment can promote the selection of new antibiotic resistances which may be transferred to pathogenic strains, which then become untreatable, there is a constant demand for new antimicrobials.



The endless cycle that illustrates the constant necessity for development of new antibiotics. The antibiotic released into the environment applies a selective stress on susceptible microbes and promotes the selection of new antibiotic resistances. The resistant strains that emerge will transmit the resistances via horizontal transfer to pathogens, thereby rendering therapy ineffective and requiring the creation of new antibiotics.

9. Cytostatic agents are designed to be very toxic (but they are also very hard to degrade). Another class of pharmaceuticals that may be found in the environment are represented by the cytostatic agents, a group of chemotherapy substances mainly used to treat cancers. Since cancer is the second most common cause of death around the world, cytostatic agents and their metabolites are extensively released in the environment. Anticancer drugs are designed to be extremely toxic for eukaryote cells causing e.g. oxidative stress, genotoxicity, cytotoxicity. The toxicity of cytostatic agents, even in trace amounts (ng L^{-1}), has been reported, so they will certainly be active in the environment.

10. Biological activity not only in humans but also in organisms living in the environment, e.g. estrogenic activity from the contraceptive pill. It is incredible how apparently non-related processes are linked by a shared fate: e.g. birth control measures in humans and the environment. The most common birth control strategy is the "contraceptive pill" which is typically composed of a low concentration of estrogens, which mimic female hormones. Once swallowed, they are partially adsorbed into the human body to execute their biological function, but the remainder is excreted intact or moderately modified into the sewage system.

The presence of the estrogens at trace concentrations in the environment, especially in water, can have adverse effects on the fish reproduction and of other water vertebrates. These "endocrine-disruptors" – hormone control disruption compounds – represent a severe problem for the aquatic wildlife and requires a better understanding of the problem in order to design new treatment strategies in wastewater treatment plants to remove such compounds.

11. Reducing fertility in humans. Then there is the issue of effect of environmental estrogens and estrogen-like chemicals on humans. Despite the growing world population, fertility rates across the globe vary enormously, with high rates in many low-income countries, and low-to-very-low rates in high-income countries. While socio-medical reasons play roles in low fertility, environmental exposures are also thought to be important. These range from environmental chemicals with hormone-like effects on humans, so-called endocrine disrupting chemicals or ECDs, to birth control hormones, to air pollution, particularly in urban settings. Both EDCs and birth control hormones find their way into wastewater and thence into surface and groundwaters.

12. How the substances may end up in the drinking water (Water cycle, from wastewater to potential drinking water). Wastewaters undergo multiple steps to remove as many contaminants as possible. Unfortunately, wastewater treatment plants are not generally designed to face a huge variety of different contaminants, including pharmaceuticals. Water from wastewater treatment plants enriched with the pharmaceuticals which have not been removed will end up in the environment (river or receiving water bodies, and thence to lakes or the sea and eventually groundwater). Moreover, pharmaceuticals administered in animal husbandry facilities will be directly discharged (intact or their degradation products) into the environment through the animal excretions. If the surface or groundwaters serve as sources of drinking water, humans can become directly exposed to the environmental chemicals they carry. While it is essential to reduce release of such chemicals into wastewater, it is equally essential to develop wastewater treatment processes that destroy them, i.e. for wastewater treatment to be an effective barrier to exposure, not only to protect humans, but also the rest of the biosphere.

Relevance for Sustainable Development Goals and Grand Challenges

- **Goal** 2. End **hunger, achieve food security and improved nutrition and promote sustainable agriculture.** Pharmaceuticals are not only applied in treating humans but also for producing meat, fish, eggs and milk. The excessive use of antibiotics in animal husbandry and aquaculture directly pollutes the environment. Here, urine and faeces will not necessarily go through wastewater treatment but will often be applied to soils.
- **Goal 3. Ensure healthy lives and promote well-being for all at all ages.** Antibiotics and other pharmaceuticals have led to a huge improvement in human health. However, they have an environmental downside. Often, antibiotics are prescribed not because they are necessary, but because a treatment is “expected” when visiting the doctor. This, in combination with the ongoing application of antibiotics to improve yields in meat production leads to an increased exposure of microorganisms to antibiotics (either in the body or in the environment). This in turn has exacerbated the proliferation of microorganisms that are resistant against numerous antibiotics, and increasing therapy failures for infectious diseases. Moreover, healthcare systems in many countries currently spend far more on pharmaceuticals to treat symptoms of widespread diseases (e.g. cardiovascular diseases) than on informing the public on how to prevent these diseases (i.e. nutrition, exercises).
- **Goal 6: Ensure availability and sustainable management of water and sanitation for all.** As the wastewater treatment process was mainly conceived decades ago to reduce *macropollutants* (organic loads, ammonium, nitrate and phosphate), it is generally inefficient in dealing with

micropollutants, such as pharmaceutical products. Furthermore, the amounts of pharmaceuticals in the wastewater of hospitals is higher than those of municipal wastewaters, where the fraction of people taking medications is lower. Hospitals and retirement homes are thus hotspots through which pharmaceuticals enter the sewage system in large amounts.

- **Goal 12: Ensure sustainable consumption and production patterns.** Nowadays, pesticides and other potentially hazardous compounds are required to enter a rigorous process to ensure that there is no accumulation in the environment, aiming at providing safe and sustainable products. However, most of the micropollutants that are problematic and hence under scrutiny are pharmaceuticals, since current wastewater treatment processes cannot remove them. Currently, there are no regulations on the biodegradability of pharmaceuticals.
- **Goal 14: Conserve and sustainably use the oceans, seas and marine resources for sustainable development.** Many pharmaceuticals end up in the oceans via contaminated freshwater bodies. While dilution in the oceans will diminish the problems, there are nevertheless local hotspots, especially where pharmaceuticals in the form are antibiotics are applied for aquafarming and in coastal areas around estuaries.
- **Goal 15: Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss.** Due to the application of pharmaceuticals in animal husbandry, there are considerable loads of polluting compounds both on soils and water bodies as well as the sewage system. In turn, it is a common practice to apply excess sludge from the wastewater treatment process onto agricultural fields as fertilizer. Due to physico-chemical processes and their accumulation in biomass, sludge will be enriched with pharmaceutical residues.

Potential implications for decisions

1. *Individual*

Patients:

a. Do not push medical professionals by specifically asking for pharmaceuticals.
b. Dispose of pharmaceuticals responsibly (do not throw them into the toilet)
c. Think about lifestyle (food, sports) to lower the probability of being dependent on medication later (“lifestyle diseases, disease of civilization”)

Medical doctors:

a. Think about consequences of prescribing pharmaceuticals too often

2. *Community/National policies*

a. Environmental pollution
b. Revision of guidelines on how wastewater should be collected and treated
c. Revision of drinking water regulations
d. Ensuring safe drinking water supplies
e. Implementation of biodegradability as a possible additional criterion for the approval/prolongation of pharmaceuticals
f. Alternatives for the application of sewage sludge as fertilizer

Pupil participation

1. Class discussion of the issues associated with pharmaceutical consumption/wastewater treatment

2. Pupil stakeholder awareness

a. Pharmaceuticals are helping a lot of sick people, but they may also have negative impact on the water that the healthy people are drinking. How could we better control which compounds end up in our water resources?

b. Are there ways of improving the results of wastewater treatment?

c. How can people stay people healthier with a better lifestyle?

3. Exercises

a. Think of strategies to safely reduce the amounts of pharmaceuticals in the waste stream (by controlling the concentrations in the system, but also the input)?

b. Can you think of possibilities to prevent high loads of pharmaceuticals from "hot spots"?

c. Can we achieve a lower consumption of pharmaceuticals? What would you do?

The viewing of a **video** regarding the possible strategies to reduce the release of pharmaceuticals into environment may promote the discussion among the pupils.

The Evidence Base, Further Reading and Teaching Aids

Video illustrating medicines in wastewater:
https://www.youtube.com/watch?v=9PTpylVotd8&t=1s

Videos illustrating wastewater treatment:
https://www.youtube.com/watch?v=FvPakzqM3h8
https://www.youtube.com/watch?v=8isr9nSDCK4

Sui Q, Cao X, Lu S, Zhao W Qiu Z, Yu G. Occurrence, sources and fate of pharmaceuticals and personal care products in the groundwater: a review. Emerg Contam 1 (1):14–24 (2015).

Nikolaou A, Meric, S and Fatta D. Occurrence patterns of pharmaceuticals in water and wastewater environments. Anal Bioanal Chem 387: 1225–1234 (2007).

How Wastewater Treatment Works...The Basics. United States Environmental Protection Agency. Office of water (4204). https://www3.epa.gov/npdes/pubs/bastre.pdf.

Revollar S, Vilanova R, Vega P, Francisco M and Meneses M. Wastewater Treatment Plant Operation: Simple Control Schemes with a Holistic Perspective. Sustainability 12 (3): 768 (2020).

Seviour R and Nielsen PH. Microbial Ecology of Activated Sludge. London: IWA Publishing Company (2010).

Nascimento AL, Souza AJ, Andrade PAM, Andreote FD, Coscione AR, Oliveira FC and Regitano JB. Sewage Sludge Microbial Structures and Relations to Their Sources, Treatments, and Chemical Attributes. Front Microbiol 9:1462 (2018).

Martín J, Camacho-Munoz D, Santos JL, Aparicio I, Alonso E. Occurrence of pharmaceutical compounds in wastewater and sludge from wastewater treatment plants: Removal and ecotoxicological impact of wastewater discharges and sludge disposal. J Hazard Mater 239–240: 40–47 (2012).

Ternes TA, Herrmann N, Bonerz M, Knacker T, Siegrist H, Joss A. A rapid method to measure the solid–water partition coefficient (Kd) for pharmaceuticals and musk fragrances in sewage sludge. Water Res. 38: 4075–4084 (2004).

Andriamananjara A, Rabeharisoa L, Prud'homme L and Morel C. Drivers of Plant-Availability of Phosphorus from Thermally Conditioned Sewage Sludge as Assessed by Isotopic Labeling. Front Nutr 3:19 (2016).

Duffus JH, Nordberg M and Templeton DM. Glossary of terms used in toxicology. Pure Appl Chem, 2nd edition (IUPAC Recommendations 2007) vol 79 no 7: 1153-1344 (2007).

Akao PK, Mamane H, Kaplan A, Gozlan I, Yehoshua Y, Kinel-Tahan Y, Avisar D. Iohexol removal and degradation-product formation via biodegradation by the microalga Chlorella vulgaris. Algal Res vol 51 (2020).

Kolvenbach BA, Helbling DE, Kohler HPE, Corvini PFX. Emerging chemicals and the evolution of biodegradation capacities and pathways in bacteria. Curr Opin Biotechnol 27: 8-14 (2014).

Kümmerer K. Pharmaceuticals in the Environment. Annu Rev Environ Resour 2010 35 (1): 57-75 (2010).

aus der Beek T, Weber FA, Bergmann A, Hickmann S, Ebert I, Hein A, Küster A. Pharmaceuticals in the environment—Global occurrences and perspectives. Environ Toxicol Chem 35 (4): 823–835 (2016).

Barra Caracciolo A, Topp E, Grenni P. Pharmaceuticals in the environment: biodegradation and effects on natural microbial communities. A review. J Pharm Biomed Anal 106: 25–36 (2015).

Deblonde T, Cossu-Leguille C, Hartemann P, Emerging pollutants in wastewater: A review of the literature. Int J Hyg Environ Health 214 (6): 442-448 (2011).

Petrie B, Barden R, Kasprzyk-Hordern B. A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring. Water Res 72: 3-27 (2015).

Marti E, Variatza E, Balcazar JL. The role of aquatic ecosystems as reservoirs of antibiotic resistance. Trends Microbiol 22: 36-41 (2014).

Lawrence JG. Horizontal and vertical gene transfer: the life history of pathogens. Contrib Microbiol 12: 255–271 (2005).

Nicoloff H and Andersson DI. Indirect resistance to several classes of antibiotics in cocultures with resistant bacteria expressing antibiotic-modifying or -degrading enzymes. J Antimicrob Chemother 71: 100-110 (2016).

Perri R, Kolvenbach BA, Corvini PFX. Subsistence and complexity of antimicrobial resistance on a community-wide level. Environ Microbiol 22: 2463–2468 (2020).

Zhang J, Chang VWC, Giannis A, Wang JY. Removal of cytostatic drugs from aquatic environment: a review. Sci Total Environ 445-446: 281-298 (2013).

Queirós V, Azeiteiro UM, Soares AMVM, Freitas R. The antineoplastic drugs cyclophosphamide and cisplatin in the aquatic environment – Review. J Hazard Mater 412 (2021).

Česen M, Kosjek T, Laimou-Geraniou M, Kompare B, Širok B, Lambropolou D, Heath E. Occurrence of cyclophosphamide and ifosfamide in aqueous environment and their removal by

biological and abiotic wastewater treatment processes. Sci Total Environ 527–528: 465–473 (2015).
Hanselman TA, Graetz DA, Wilkie AC. Manure-borne estrogens as potential environmental contaminants: A review. Environ Sci Technol 37 (24): 5471—5478 (2003).

Glossary

Biological recalcitrance: tendency of a compound to resist to biodegradation process

Ecotoxicology: science that study and quantify the negative effects of chemicals or materials to living organisms (including plants) in the environment

Antimicrobial resistance: capacity of microorganisms to avoid being affected by compounds that aims to kill them or slow down their growth

Non-target effects of pharmaceuticals: additional unwanted effects of medicines aimed to treat a given illness

Steroids: family of anti-inflammatory medicines

Fate: series of processes (biological, physico-chemical) that affect a chemical in the environment

Bioactive molecules: molecules that exert effects on living organisms

Metabolised: « degraded »

Metabolites: transformation or degradation product of a given substance

Enzymes: biological molecules (proteins) that are able to transform a chemical into another chemical product. One talks about enzymatic reaction

Genes: piece of genetic information that procures a given trait in living organisms

Oxidative stress: stress caused by very reactive molecules, which interfere with normal functions in living organisms

Genotoxicity: adverse effects on hereditary biological information material (.i.e. DNA)

Cytotoxicity: adverse effects on the cells of living organisms.

Hormones: are small molecules in higher organisms (human, plants, etc.) that are involved in the regulation of certain functions, e.g. need to sleep