Wastewater-borne Contaminants of Emerging Concern: *Challenges and Opportunities in Evaluating and Protecting Ecosystem Health*

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Abstract

Purpose of Review: This review aims to identify the challenges in dealing with a growing list of wastewater-borne pollutants, various treatment technologies employed to remove legacy contaminants (metals, nutrients, pesticides, pathogens) and Contaminants of Emerging Concern (CECs) in WWTPs, and the consequences to ecosystem health if wastewater is not properly managed. The groups of CECs discussed include pharmaceuticals and personal care products (PPCPs), endocrine disrupting compounds (EDCs), and per and polyfluoroalkyl substances (PFAS). Future research needs and possible solutions are also discussed.

Recent Findings: Different treatment technologies are being evaluated for effective treatment of varying groups of CECs, and it's becoming clear that different contaminants require different technologies for successful treatment. With such a large number of CEC compounds out there, this will ultimately make the treatment process less cost-effective and more difficult.

Summary: WWTPs were not originally engineered to treat CECs. We're now discovering that CECs are constantly encountered in our environment as a result of inadequately treated wastewater discharge and are also toxic and persistent. Wastewater treatment technologies that are currently in place are effective in some cases in removing some of these contaminants, but not all. With such a large number of contaminants, generally present in the environment in mixtures, it is a challenge to conduct the representative toxicity studies that are needed to enact environmental regulations and policy at the state and federal levels. Though research is ongoing, there is still a lot to learn regarding toxicity, remediation, and wastewater treatment technologies for CECs.

Keywords: Contaminants of Emerging Concern, PFAS, Endocrine Disrupting Compounds

Wastewater Treatment

1. Introduction

Municipal or domestic wastewater originating from households contains various contaminants such as nutrients, metals, pathogens, and contaminants of emerging concern (CECs). Municipal wastewater is largely managed by centralized wastewater treatment plants (WWTPs) in developed countries where wastewater from a large population is collected, generally treated for biological oxygen demand (BOD), nutrients, and parasites, then discharged to surface waters or the ocean [1, 2]. In the US, for example, 80.4% of surveyed households reported use of a centralized wastewater treatment system and only 19.6% reported using a decentralized water treatment system at their home [3]. In many developing countries where resources are scarcer and technical expertise may be lacking, wastewater is often not treated or is only minimally treated before discharging [4, 5]. Thus, wastewater-borne contaminants such as nutrients, pathogens, and metals are still the leading cause of many widespread problems in Africa and southeast Asia [6]. However, the release of contaminated wastewater occurs in both developing and developed countries alike. The problem of inadequately treated wastewater is complicated by the emergence of contaminants that are not well understood and can be toxic in trace concentrations, and which appear to be globally widespread [7-9]. Understanding the fate, transport, degradation, and transformation processes, and potential toxicity of CECs is important for protecting ecosystem health and ensure the future of sustainable wastewater.

This paper aims to identify the challenges in dealing with a growing list of wastewater-borne pollutants, various treatment technologies employed to remove legacy contaminants (metals, nutrients, pesticides, pathogens) and CECs in WWTPs, and the consequences to ecosystem health if wastewater is not properly managed. The groups of CECs discussed include pharmaceuticals and personal care products (PPCPs), endocrine disrupting compounds (EDCs),

and per and polyfluoroalkyl substances (PFAS). Although EDCs may be a subset of both PPCPs and PFAS, they are discussed separately here because they typically appear as a separate group of CECs in the literature and the mode of action of EDCs in terms of biological toxicity is distinct from the other two groups.

2. Wastewater Management and Treatment in the World

Wastewater collection and treatment methods vary significantly throughout the world depending on treatment requirements and regulations, location, economic factors, population size, and social constraints [4, 10, 11]. However, these methods can generally be divided into two groups: centralized treatment systems and decentralized treatment systems. Centralized systems are typical in developed nations, especially in areas that are densely populated. The foundation of the centralized treatment system is that wastewater is carried away from the home or business through a central collection system which consolidates the wastewater and transports it to a WWTP [1, 12]. Wastewater is then treated according to applicable regulations and commonly discharged to a nearby surface water body or applied to the land surface [2]. Though centralized systems are known to be a highly effective means of sanitation, the necessary infrastructure and management required for these systems is quite costly [13]. Centralized systems also rely on potable drinking water to transport waste, which may be a significant drawback in areas where clean drinking water is scarce [14]. As the human population continues to increase, clean drinking water will become even more limited and using clean drinking water for applications other than actual drinking may no longer be feasible.

Wastewater treatment in WWTPs is generally achieved by a combination of physical, biological, and chemical processes [2, 15]. Physical processes help to remove solids and debris

from the wastewater through filtration and gravity settling. Biological treatment utilizes microorganisms to break down the high levels of organic matter typical of untreated wastewater and transform nutrients. Chemical processes are generally used for disinfection of the wastewater prior to discharge. Common treatment technologies such as trickling filters or activated sludge depend on the biodegradation processes utilized in WWTPs. Trickling filters are capable of establishing a stable microbial population over time, whereas activated sludge systems are less able to maintain stable populations because particular microbial species can be washed out of the system [16]. Chemicals used to disinfect wastewater (through chlorination) and remove harmful pathogens can improve the physical separation of pollutants present in the wastewater [2]. As an alternative to chlorination, ozone and ultraviolet radiation can also be used to remove pathogens from wastewater prior to discharge [17, 18].

In contrast, decentralized systems tend to be utilized more frequently in developing nations and in more remote or suburban areas that lack centralized systems due to economic feasibility. A decentralized system can be described as a wastewater collection and treatment system where the wastewater remains untreated or is treated at the site of generation before being discharged [1]. Wilderer and Schreff [12] define a decentralized system in terms of the collection system, which employs a less complex collection system than a centralized system and the pipes for collection are generally shorter in length or non-existent. Decentralized systems can range from the most isolated treatment systems servicing only one property, such as pit latrines and composting toilets, to larger cluster systems that may service several different properties or communities [1]. Constructed treatment wetlands are considered an adequate alternative to large centralized systems for wastewater treatment in developing nations, though because of the critical role that biotransformation and plant growth play in wetland processes, they tend to be

much more effective in countries with tropical climates [19]. The most common decentralized system in the United States and other parts of the world is known as a septic system or onsite wastewater treatment system, which consists of two parts (1) a septic tank that collects and stores wastewater from the household and (2) a drainfield that discharges wastewater via a series of trenches or pipes in the sub-surface soil [20].

Although decentralized systems are more likely to be employed within developing countries, they are also utilized in many developed nations around the world such as Japan, Australia, and Italy [1, 21]. This is partially due to the flexibility of such systems but also that some communities just don't have access to a centralized system and must treat their wastewater. Additionally, they have been proven to be at least as effective as centralized systems if properly managed, and for some CECs may be even more effective [14, 1]. Decentralized systems also have a greater potential for wastewater reuse and recycling at the site of generation, and the water can be reused for irrigation of crops, landscape irrigation, toilet flushing, or groundwater recharge depending on the level of treatment [22, 15]. Concerns about access to clean water in the world are increasing as a result of global climate change, and water treatment systems that focus on sustainability and reuse will become necessary and may provide solutions to meet the water needs of a growing population [6]. Decentralized systems generally rely on the same processes for treatment as a typical centralized system, but are implemented on a smaller scale. In some developing countries wastewater treatment systems are extremely rudimentary to almost non-existent; in these areas local communities still struggle with legacy contaminants such as nutrient pollution and exposure to pathogens and access to clean drinking water [23-26]. Further, human health and ecological risks related to CECs are not a priority or even considered when addressing sanitation issues in developing countries. To date, the US Clean Water Act does not

regulate any CECs under National Pollution Discharge Elimination System (NPDES) permits [27]. The typical WWTPs are not designed to treat many of the CECs that are currently the focus of environmental research in developed nations, and therefore are generally not very effective in removing these contaminants [14].

3. Wastewater-borne Contaminants

3.1 Legacy Contaminants: nutrients, metals, pesticides

Historically and still today, WWTPs in developed countries are designed to treat only for BOD, nutrients such as nitrogen (N) and phosphorus (P), total suspended solids (TSS), and pathogens such as Escherichia coli (E. coli) prior to wastewater discharge and reuse. These contaminants are referred to in this review as 'legacy contaminants'. Such contaminants in discharged effluent are regulated in the United States under the 1972 Amendments to the Federal Water Pollution Control Act (33 **U.S.C.** §1251 et seq. 1972), also known as the Clean Water Act, by the National Pollutant Discharge Elimination System permit. This permit requires monitoring of certain contaminants in wastewater and receiving water bodies to ensure water quality and aquatic community protection [2].

Excessive N and P, the most common nutrients present in wastewater worldwide, can lead to diminished water quality, eutrophication, onset of harmful algal blooms, and hypoxia in aquatic systems if wastewater is not properly treated prior to discharge in water bodies [28]. The negative effects of improperly treated nutrients on aquatic ecosystem health are exacerbated by other major sources of N and P such as agricultural practices and fertilizer use [29-31]. Heavy metals (Cd, As, Pb, Zn, Cu, etc.) have also historically been problematic when treating wastewater, and are known to interfere with ecosystem function, bioaccumulate in wildlife, and

can be toxic to human health [32-36]. Metals are conventionally removed from wastewater through the activated sludge process, chemical precipitation, or ion exchange processes used in modern WWTPs [37]. Although the activated sludge process is effective in removing heavy metals from wastewater, the metals tend to accumulate in the sludge, which is then commonly applied to the land and over time can accumulate in agricultural fields where repeated applications of sludge have occurred [38, 39].

Wastewater effluent may also be a source of pathogenic microorganisms to the environment, which originate from fecal matter [40]. Pathogens such as E. Coli, Cryptosporidium, and Giardia lamblia are regulated by the EPA in drinking water and wastewater discharge. WWTPs typically treat pathogens using a method of disinfection or deactivation, which render the pathogens harmless (EPA, 2015). According to the EPA (2015), the most common treatment methods for pathogenic microorganisms are chlorination, ozonation, and ultraviolet radiation [41].

3.2 Contaminants of Emerging Concern: PPCPs, EDCs, and PFAS

3.2.1 Pharmaceuticals and Personal Care Products

PPCPs are a group of compounds that have gained recognition as environmental contaminants over the past decade, and are now generally considered under the umbrella of CECs [42]. Pharmaceuticals are chemicals that are used to treat, prevent, or diagnose diseases in humans and animals and include both prescription and over-the-counter drugs and their metabolites, including antibiotics, lipid regulators, analgesics, antidepressants, anti-epileptics, amphetamines, beta-blockers, and antiseptics [43]. Many illicit drugs such as 3,4-methylene-dioxy-methamphetamine (MDMA) and cocaine are also included in this category. Personal care products generally refer to products used by humans to improve quality of life such as soaps, hair

products, makeup, moisturizers, perfumes and fragrances, and sunscreens. There are currently more than 4,000 PPCPs in use today [44], which is a particular challenge when assessing the potential presence and risk of these compounds in the environment. Some of the compounds within the PPCPs group may overlap with those in the endocrine disruption compounds (EDCs) group. However, a review of the literature indicated that PPCPs and EDCs are typically discussed separately [16, 8] likely because of the differences in how these compounds are metabolized by biological organisms and their specific modes of action.

The most significant source of PPCPs in the environment is wastewater from WWTPs, as PPCPs are excreted with human waste or washed down the drain after being used or ingested [8, 42]. They are typically detected in concentrations ranging from ng/L (parts per trillion) to µg/L (parts per billion) in both raw wastewater and treated wastewater [42]. Studies have been conducted worldwide on the presence of PPCPs in wastewater, and a review of the literature by der Beek et al. [45] showed that diclofenac (a non-steroidal anti-inflammatory drug) was the pharmaceutical most frequently detected. Significant concentrations of caffeine, analgesics, antibiotics, antidepressants, and various other PPCPs have also been detected worldwide in aquatic systems affected by wastewater discharge from WWTPs [46, 47, 8, 42, 16, 45]. Antivirals and antibiotics were reported to be present in higher concentrations in wastewater in parts of Africa due the prevalence of HIV relative to other areas of the globe [48]. Such correlations with usage and consumption were also noted in a study of PPCPs in south Wales, United Kingdom, where the authors reviewed the prescriptions dispensed in the communities, databases compiling household product usage, and estimations of illicit drug use and concluded that usage patterns were linked to concentrations in wastewater [16]. This same study also demonstrated that concentrations of PPCPs in receiving waters depend on wastewater flow,

which is affected by dilution and rainfall; drier conditions tend to create lower wastewater flows and increase the concentrations of PPCPs in receiving waters [16, 49]. This is true only to an extent, however, as excessive rainfall could overwhelm sewer capacity and lead to Combined Sewer Overflows (CSOs), which can potentially discharge untreated wastewater into waterways increasing the concentrations of PPCPs and other CECs in the aquatic environment.

A study of wastewater effluent samples throughout the US showed that metoprolol, atenolol (both beta-blockers), and carbamazepine (anticonvulsant) were detected in over 90% of the 50 samples collected [50]. Valsartan (antihypertensive) was detected in wastewater effluent in this study at concentrations as high as 5.3 µg/L. Carbamazepine was frequently detected in WWTP effluent at concentrations ranging from 0.5 to 1 µg/L in Calgary, Alberta, Canada [42]. In reclaimed waters from WWTPs in China, sulpiride, an antipsychotic used to treat schizophrenia, was the most frequently detected PPCP with a high concentration of 470.8 ng/L [8]. Li et al. (2015) and a review of other similar studies in China, indicate that such frequent detections of sulpiride are typical in China [51, 52]. Sulpiride is not approved for use in the US and therefore has not been studied in WWTP effluents in the US. Illicit drugs such as MDMA and cocaine have been detected in surface water in the UK at concentrations of 25 ng/L and 17 ng/L, respectively [53]. They also compiled sampling data related to PPCPs throughout the UK in WWTP influent, effluent, and surface waters and found that highest concentrations in treated effluent consisted of tramadol (59.05 µg/L), atenolol (2.87 µg/L), caffeine (2.048 µg/L), and triclosan (0.2 µg/L). This is just a small sampling of examples from the literature, but demonstrates that PPCPs in wastewater are a global issue and that concentrations of such compounds are significant and widespread.

WWTPs are not designed to remove PPCPs [42]; however, some WWTPs, depending on the technologies employed, can successfully remove a select handful of PPCPs. On the other hand, these same processes have also been reported in some cases to increase the concentration of certain PPCPs in WWTPs [16]. The two most frequently evaluated WWTPs technologies relative to PPCP removal are trickling filters and activated sludge. Activated sludge was reported to be more effective for overall PPCP removal than trickling filters, although both represented significant overall removals of 50–85% and 50–70% PPCP removal, respectively [16, 49, 54]. Petrie et al. (2015) reported a broad range of overall removals from below 50% to over 80% for PPCPs in WWTPs. Some PPCPs had very high removal rates, such as caffeine, amphetamines, aspirin, and salicylic acid [16, 49, 54], and other PPCPs highly resistant to treatment include carbamazepine and diclofenac [16, 55, 8, 42]. Treatment effectiveness and overall removal are highly dependent on a variety of parameters, however, and there are exceptions to these generalizations.

The fate of PPCPs, and most CECs, is strongly influenced by sorption mechanisms, although it has been demonstrated that generalizations regarding adsorption to solids such as river sediments using K_{ow} (octanol water distribution coefficient) values are not always entirely accurate and can depend on a range of parameters [56, 57]. Effective removal of CECs in WWTPs depends on climate, chemical and physical properties of the individual compounds, treatment technologies applied, and the retention time [49, 54]. The primary removal mechanisms for PPCPs are biodegradation and adsorption, although it is often not known which mechanism dominates because the literature on this subject tends to focus more on dissolved phase concentrations in WWTPs influent and effluent while neglecting the concentrations adsorbed into the sludge [58]. For example, a study in the United Kingdom demonstrated that

removal of almost 90% of antidepressants with activated sludge was due to the partitioning to solids [49]. Triclosan and triclocarban are also reported to be enriched in sludge relative to wastewater [59]. This highlights the importance of examining both the aqueous and solid compartments of WWTP effluents when evaluating the fate of CECs.

Abiotic photodegradation, though less commonly used in WWTPs, has been proven to be an effective removal mechanism for several PPCPs, including diclofenac and propranolol [60]. They evaluated the effectiveness of photodegradation for PPCPs and found that, under the same solar and climatic conditions, diclofenac had a half-life of 5 days whereas carbamazepine had a half-life of approximately 100 days. Furthermore, a study on river sediments in Florida that had been impacted by wastewater effluent found that carbamazepine was detected at a 100% frequency, whereas diclofenac was not detected at all [57]. Another study in Berlin, Germany looked at the effectiveness of powdered activated carbon and ozonation as alternative treatment technologies for the recalcitrant diclofenac and carbamazepine. The results indicated over 90% removal efficiency for both compounds using both technologies [61]. As these two PPCPs are highly resistant to degradation in standard WWTPs, these studies underscore the value in examining atypical removal processes for CECs.

3.2.2 Endocrine Disrupting Compounds

Another group of compounds that are gaining recognition in the environmental community as potential contaminants discharged from WWTPs are EDCs. These compounds disrupt the endocrine system, or otherwise interfere with normal endocrine system functions [42]. The harmful effects of EDCs have been studied in wildlife for many decades [9], but more recently EDCs have been identified as wastewater-borne contaminants. In the environment, individual

EDCs are typically present in lower concentrations (in the range of ng/L) but their effects are likely additive [62] making mixtures of EDCs potentially toxic. A few examples of EDCs commonly studied in relation to wastewater from WWTPs include dichlorodiphenyltrichloroethane (DDT), bisphenol- A (BPA), estrone, estradiol, estriol, progesterone, triclosan, phthalates, and alkylphenols [63-65, 42, 9].

EDCs have been detected worldwide in a variety of aquatic systems that receive or are impacted by WWTP effluent. For example, a study on EDCs related to WWTP effluent in Minnesota, USA found that nonylphenol, which is a breakdown product of detergents and mimics estrogen in the endocrine system, was detected most frequently, in 80% of the wastewater effluent samples collected in the study (up to 10 µg/L), whereas BPA was detected in 56% of effluent samples. 17β-estradiol was detected in 100% of sediment samples collected downstream of the effluent discharge [66]. A comparative study that examined EDCs in WWTP effluent discharge in two different stream systems in Iowa and Colorado found that triclosan was present in both effluents and also persisted downstream from the discharge point in both streams indicating that dilution, natural degradation, and sorption processes were not effective in removing triclosan in either system [62]. They also found that 4-nonylphenol and 4-nonylphenolethoxycarboxylic acid (NPEC) were detected in WWTP effluent at concentrations as high as approximately 1 µg/L and 100 µg/L, respectively. A study of several WWTPs in Turkey detected estrone and progesterone in effluent at concentrations up to 58 ng/L and 8 ng/L, respectively [65]. A study in China that examined reclaimed wastewater and groundwater (which had been recharged with the treated wastewater) found BPA in 100% of the groundwater samples analyzed at concentrations up to 35.54 ng/L, and was detected at concentrations of up to 95.7 ng/L in reclaimed wastewater [8]. They also detected estriol, 17α-ethinylestradiol, and 17β-

estradiol at fairly high detection frequencies in both groundwater and treated wastewater. Alkylphenolic EDCs were studied in the receiving streams in the greater metropolitan Chicago area, where all of the compounds analyzed were detected in all samples [63]. This included 4-nonylphenol, BPA, triclosan, NPEC, and ethylenediaminetetraacetic acid (EDTA), with EDTA and NPEC detected at the highest concentrations.

As with PPCPs, removal efficiency of EDCs in WWTPs is highly variable and depends on the chemical and physical characteristics of the compound, the hydraulic retention time of the wastewater in the WWTP, and the specific technologies employed at the facility [67-69]. For many of the EDCs studied, conventional WWTPs technologies such as activated sludge and trickling filters are reported to be somewhat effective in removal. In Turkey, Komesli et al. (2015) compared a medium-capacity membrane bioreactor facility and five different WWTPs, all of which had different capacities and slight variations of conventional activated sludge treatment technologies. They found that progesterone and estrone were generally reduced in most conventional facilities. Removal efficiencies of EDCs for conventional WWTPs were reported to be much greater than those for the membrane bioreactor plants. Estrone, a natural hormone, was found to have a removal efficiency that ranged from 0 to100% in the WWTPs studied by Komesli et al. [65]. In some of the WWTPs, estrone was accumulated in sludge, whereas in others estrone was absent from sludge samples. The only differences noted by Komesli et al. between these WWTPs were the geographic location, indicating that climate may play a role in treatment efficiency of estrone. In this same study, the accumulation of progesterone in sludge appeared to be affected by residence time where progesterone tended to be absent from sludge samples in plants with residence times greater than 17 days.

Sorption plays an important role in the removal of triclosan and 4-nonylphenol, as both compounds are hydrophobic with relatively high octanol/water partition coefficients of log K_{ow}=4.2 and log K_{ow}=4.8, respectively [62]. Generally speaking, estrogens tend to have higher octanol/water partition coefficients and therefore will sorb more readily to organic material [54]. Hydraulic retention time has also been reported to be important in the removal of hydrophobic EDCs such as estrogen [54]. When sorption is expected to be the mechanism of removal, as it is with these compounds, sewage sludge may need to be treated if it is to be reused or applied to the land due to EDC accumulation [65].

In a study in the UK that compared activated sludge and trickling filters for a variety of EDCs, it was found that overall activated sludge was a more effective treatment technology than trickling filters. However, this study determined that for BPA, trickling filters (91% removal) were more effective than activated sludge (85%) [16]. This study also noted differences in removal efficiencies relative to flow conditions within the WWTPs, though it was not able to draw definitive conclusions regarding the reasoning for such variation. In a study in Brazil that compared activated sludge, anaerobic sludge blanket reactors, and stabilization lagoons, BPA had nearly 100% removal efficiency for each of the three technologies [54].

Compounds that are resistant to biodegradation, such as EDTA, may be degraded through photolysis processes. In a study comparing two receiving streams in Colorado and Iowa, EDTA attenuation was reported to be higher in the Colorado stream with less turbidity and greater light penetration [62]. Incorporating such mechanisms into standard WWTPs may help to reduce or eliminate biologically recalcitrant CECs prior to discharging in aquatic systems.

3.2.3 Per and Polyfluoroalkyl Substances (PFAS)

PFAS are a group of man-made organic compounds that are recognized for their extraordinary properties and are used in many products such as textiles, fire-fighting foams, non-stick cookware, waterproof clothing, electronics, carpets, processed food wrappers (such as the non-stick lining in typical microwave popcorn bag), mist suppressants, and photography equipment and film [70, 71]. In recent years, PFAS have become more widely known for their presence in WWTP effluent and their potential to threaten ecosystem health [72, 73]. The two most common PFAS are perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), though there are many other PFAS in use today with varying chemical structures and carbon chain lengths. The uses of these chemicals are far-reaching and affect a wide range of global industries, which explains their ubiquitous presence in environments around the world [74].

PFAS have been detected worldwide in wastewater at concentrations of up to a few hundred ng/L [75]. In WWTP effluent from eight facilities that discharged to the San Francisco Bay, 15 different PFAS were detected in all effluent samples [76]. Median concentrations of PFOS and PFOA found in these effluent samples were 15 ng/L and 23 ng/L, respectively. They also demonstrated that between 2009 and 2014, PFOS and PFOA concentrations decreased in WWTPs effluent, whereas other shorter chain PFAS increased in average concentration. This may reflect current manufacturing and usage trends, as PFOS and PFOA are being phased out [7] and replaced with shorter chain PFAS [76]. In the Lake Victoria basin in Kenya, PFOS and PFOA were detected in WWTP sludge at concentrations as high as 611 and 256 pg/g, respectively, and in wastewater effluent at concentrations up to 9.8 and 23 ng/L, respectively [77]. Elevated concentrations of PFOS (up to 128 ng/L) in the Jucar River in Spain have been attributed to WWTP discharge [78]. It should be noted that in the above-mentioned studies, various PFAS other than PFOS and PFOA were also detected.

A common removal process for contaminants in WWTPs is biodegradation; however, studies have demonstrated limited biodegradation of PFAS in WWTPs. Kwon et al. (2014) demonstrated the somewhat successful aerobic biodegradation (67% decrease) of PFOS by *Pseudomonas aeruginosa* [79]. Another study which examined anaerobic biodegradation for PFOA was unable to identify a microbial mechanism or organism that could degrade the compound [80]. Though biotransformation does not seem like a viable mechanism for removal of PFAS in wastewater, the review by Arvaniti and Stasinakis (2015) on PFAS removal in wastewater suggests that advanced technologies such as granular activated carbon, powdered activated carbon, nanofiltration, phytolysis, and reverse osmosis may be promising for the future of wastewater treatment for PFOS and PFOA [75].

Schultz et al. (2006) evaluated the effectiveness of a full-scale WWTP in removing PFAS, which included PFOS and PFOA in the Pacific Northwest region of the U.S. They collected samples throughout each step of the 'lifecycle' of wastewater in the WWTP, which included a primary clarifier, a trickling filter, activated sludge aeration basins, secondary clarifiers, chlorination and dechlorination, and ultimate discharge to a surface water body. The study demonstrated that this standard WWTP had no effect on PFOA and therefore was not effective in reducing the PFOA concentrations in wastewater before discharge to the river. The more interesting finding, however, was that the mass flow of PFOS actually increased as the compound moved through the WWTP. They postulated that this was a result of the biodegradation of PFOS precursor chemicals that were present in the raw influent [81]. Thus, it could be argued that standard WWTP processes may be insufficient in many instances at removing PFAS from influent, and may have the opposite effect of increasing concentrations in treated wastewater.

4. Effects of Contaminants of Emerging Concern on Ecosystem Function

As CECs exist in treated wastewater all over the globe, it is not surprising that these chemicals are beginning to play a role in the ecosystems impacted by contaminated wastewater. Studies have detected CECs in the tissues of birds, fish, and livestock, as well as plant roots, crops, and human blood, though toxicity data and effects are still limited in the literature [82, 83, 74, 84, 59]. Of the studies that are available, the conclusions are unsettling as documented negative effects include fish feminization, renal failure and near species extinction in birds, diminished immune response, and decreased xenobiotic metabolism [85, 86].

The negative effects of CECs on fish species are apparent in several studies conducted in lakes and streams impacted by contaminated wastewater. A good example of this is a study conducted on white sucker and fathead minnow fish in Boulder Creek, in Boulder, Colorado, where treated wastewater makes up to 75% of the stream flow [87, 88] and wastewater is contaminated with EDCs such as 17β-estradiol, estrone, 4-nonylphenol, and 17a-ethynylestradiol. They compared exposed fish downstream of the wastewater treatment plant to unaffected fish from a reference upstream site and found that 83% of white suckers were female in the portion of Boulder Creek affected by the wastewater, whereas upstream fish populations were composed of 45% female [88]. Further, the exposed fish showed signs of reproductive disruption and demasculinization/feminization such as decreased sperm abundance, fewer and less prominent nuptial tubercles, less prominent dorsal fat pads, and elevated plasma vitellogenin. This same study also assessed white sucker populations downstream of another WWTP in Colorado, and only female and intersex fish (where gonads are a mix of both male and female tissues) were reported; males were not found.

PFAS are known to be stable in the environment and are generally not metabolized by organisms. They are known to interfere with fatty acid and glucose metabolism, cell membrane function, intercellular communication, and mitochondrial functions in organisms [89]. Lau (2007) reviewed multiple studies on PFAS demonstrating neurotoxicity, immunotoxicity, developmental toxicity, tumor induction, hepatotoxicity, and even instances of endocrine disruption, although most of these studies were conducted on laboratory rats and mice. In the natural environment, outside the tightly controlled conditions of the laboratory, PFAS have been found in a wide range of species. In several lakes in Minnesota which had been impacted by PFAS-contaminated WWTP effluent, largemouth bass exhibited disruptions of xenobiotic metabolism, protein degradation, and diminished immune responses [86]. Of all the different PFAS studied by Colli-Dula et al. (2016), PFOS was detected at the highest concentrations in the largemouth bass and it was noted that PFAS differentially accumulate in fish organs. A study on northern leopard frog tadpoles in Indiana demonstrated how the uptake of PFAS can depend on duration of exposure, exposure concentration, and compound type [90]. Developmental delays were noted for all tadpoles exposed to any PFAS compound, though PFOS and PFHxS (perfluorohexane sulfonic acid) were found to cause the most significant developmental delays. This same study also found that PFOS had the highest accumulation concentrations in body tissue for tadpoles. PFOS and PFHxS concentrations are interesting because as of 2002, major manufacturers of these compounds have phased out production in the US due to their significant toxicity and prevalence [91]. A study in the San Francisco Bay aimed to track the impacts of this phase-out by measuring PFAS concentrations in bird eggs and seals over time. PFOS concentrations in seals and bird eggs from this study were found to be significantly higher than any other PFAS during all sampling events; however, the study suggests that PFOS

concentrations in wildlife have generally declined over the study period between 2004 and 2014 following the phase-out of this chemical in 2002 [84]. This San Francisco study did report a significant lag time (12 years) in the eventual decline of PFOS detected in seals from the South Bay area after the 2002 phase-out, approximately twice as long as similar notable decreases reported in Iceland, Germany, and Canada demonstrating that there are many factors that can influence uptake, bioaccumulation, and persistence of these compounds in the environment. A review by Houde et al. [92] suggests that temporal trends for PFOS following the phase-out are murky, and vary significantly among species, location, exposure, and uptake path, and that it may be difficult to discern such trends accurately without regular long-term sampling.

5. Challenges and Opportunities for Future Research

The challenges presented by CECs in the environment are many, and are further compounded by the complexity of natural ecosystems. It was never intended that CECs would reach aquatic ecosystems, but as has been established throughout this review, CECs are near ubiquitous as a result of inadequately treated wastewater discharge and they are toxic and persistent. Consistent sampling design and analytical procedures for CECs in WWTP influent/effluent are needed to generate representative datasets. The data cited in this review were collected using a variety of sampling designs and techniques which can make it difficult to compare studies or compile a comprehensive database. A review by Ort et al. [93] examined the variability in the distribution of PPCPs in wastewater systems and how to select an appropriate sampling design for the most representative dataset. Ort et al. explain how WWTP influent is heterogeneous in its concentrations of contaminants as different parcels of wastewater are delivered to the WWTP in punctuated loads rather than one continuous homogenized stream, which demonstrates the

importance of collecting multiple samples rather than just one 'snapshot' sample in time. It would be beneficial to capture seasonal changes over the course of a year, weekday/weekend variations, as well as changes throughout a 24 hour period. In a review of published studies on PPCPs in rivers, it was found that only 11% of studies implemented a sampling strategy that employed composite sampling or repeated grab sampling to capture the heterogeneous nature of contaminant loads [46]. The review by Ort et al. encourages an evaluation of each proposed wastewater contaminant study on a case-by-case basis as each sewer catchment system has unique characteristics, and study design may be compromised if they are structured around the convenience or availability of a sampling device or analytical method. This may be problematic for many studies limited by funding where the more convenient or available methods may be the only options, potentially yielding unrepresentative results. The U.S. Department of Defense Environment, Safety, and Occupational Health Network and Information Exchange (DENIX) recently released a fact sheet titled *Bottle Selection and other Sampling Considerations When Sampling for PFAS*, which outlines the recommendations for water sample collection and handling for PFAS; the fact sheet is a laundry list of prohibited items, required equipment, and outside sources of contamination [94]. This fact sheet is not widely distributed and the recommendations are inconvenient for the average water sampling team, making such practices less likely to be implemented in the field. These limitations lead to a lack of reliable data in the published literature, which could be a hindrance to further research and innovation.

The current lack of toxicity information on CECs is another roadblock to effectively protecting ecosystem health and the environment. It is clear that these chemicals are toxic at commonly reported concentrations in impacted water bodies, but the specifics are murky. Establishing the toxicity of a chemical is a long, iterative process, but is necessary to establish

enforceable regulatory concentration limits at both the federal and state levels. With an abundance of CECs in the environment, it is a challenge to study each and every chemical to come up with reliable toxicity data. An added complication is that CECs are almost always present in WWTPs as mixtures of chemicals, which can alter their toxicity, mode of action, and tendency to degrade. Modeling of EDCs on the river catchment scale has been proposed to evaluate the risk of these chemicals to aquatic systems affected by contaminated WWTP effluent, and stresses the utility of a model for EDC risk assessment as opposed to directly measuring concentrations in water, sediment, and tissue [95]. The model is based on a well-established hydrologic model known as GREAT-ER, and can account for the additive effects of mixtures of EDCs. A study on an impacted stream in China verified the use of this model for nonylphenol [96]. Modeling may help bridge the gap in protective risk assessment between what we know now and the future, when presumably we will be better informed on the precise risks associated with CECs.

For as long as it takes to establish reliable toxicity data, the legislation and policy-writing of regulatory agencies can be an even longer and more convoluted path. The US Clean Water Act (33 **U.S.C.** §1251 et seq. 1972) is intended to regulate pollution discharge to surface water bodies from point sources, such as those discharged from WWTPs. Aquatic life criteria are an important component of the Clean Water Act, and the US EPA has established requirements designed to protect aquatic organisms from toxic pollutant discharge [97]. These criteria are discussed in detail in EPA's 1985 *Guidelines for Deriving National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses*; however, because of its earlier date of publication it does not account for many of the CECs that we are dealing with in surface water systems today. EPA recognized this, and in 2008 a scientific advisory board was convened to

discuss how the 1985 guidelines could be modified to include emerging contaminants such as EDCs and PPCPs (EPA, 2008). The effort has not produced any formal guidance by EPA on the issue of CECs and deriving numerical criteria for aquatic life (though a draft White Paper can still be found on their website), but it is clear that this was a serious topic of discussion within the agency. It is an evolving issue, but again, continued research on the fate, transport, and toxicology of these CECs will help to clear up some of the uncertainty.

In 2016, the US EPA established a 'drinking water health advisory' level of 70 μg/L for PFAS, which is noted to be a combined concentration of PFOS and PFOA, the two most common PFAS. An EPA health advisory is not an enforceable standard or a regulatory requirement, but rather just a guideline, which is thought to reasonably provide protection from lifetime exposure to PFOS and PFOA (EPA, 2016). States can either choose to adopt such advisories or not. New Jersey, for example, has established a maximum contaminant level of 14 μg/L for PFOA and 13 μg/L for PFOS, much lower than the EPA health advisory. Other states, such as Wyoming, have established no such risk-based standard for PFAS, and generally are not even testing for these chemicals at contaminated sites where they are likely to be present. It is in states like Wyoming where the establishment of an enforceable standard by EPA may be beneficial to environmental and human health protection and in order to do this, more definitive toxicity research is needed. EPA's health advisory was informed by toxicity studies on laboratory animals and a few epidemiological studies on humans. Although additional toxicity research is still needed, the release of a health advisory limit by a federal regulatory agency indicates that research efforts are progressing, paving the way towards enforceable, more reliable regulatory standards.

6. Conclusions

Threats to aquatic ecosystems by inadequately-treated WWTP discharge is a global concern that requires a multi-faceted approach to fully address, beginning with manufacturing and production. The voluntary phasing out of certain CECs by manufacturing corporations has been reasonably effective as a partial solution to the problem. However, for this to be truly effective, it needs to be managed on a global scale. The PFOS phase-out in the US was compensated for by increasing production in other countries overseas. This only shifts the burden to other continents where environmental regulations are more relaxed. Another thing to be aware of is that when the manufacture of one compound is discontinued, it is likely to be replaced with another similarly-acting compound, and oftentimes these replacement chemicals have not been fully vetted environmentally and toxicologically. The history of BPA is a perfect example of this: BPA was reported to be a toxic EDC used in many consumer plastic products and was banned in baby food and drink containers by the US Food and Drug Administration in 2012. The removal of BPA prompted the use of substitutes, such as Bisphenol-S (BPS) and Bisphenol- F (BPF), which are now known to have similar adverse estrogenic activity [98]. The review by Rochester, et al. describes this as a case of "regrettable substitutions", or compounds that were not adequately evaluated for toxicity prior to full-scale market use and ultimately turn out to be just as harmful as the chemicals they were intended to replace. Furthermore, some consumer products labeled BPA-free were found to leach chemicals having even greater estrogenic activity than BPA [99].

At the WWTP level, it is necessary to start incorporating CECs into the treatment processes that are built to address legacy contaminants. This will involve some creative problem-solving and modifications that aim to reduce the concentrations of CECs to the extent practicable prior to discharge, while being cost-effective and appropriate for the communities in which they are

located. This will be a challenging, long-term task requiring careful considerations and innovative solutions.

Additional toxicity research will fuel informed regulatory intervention in all of these processes, from manufacture and production, to wastewater treatment, to discharge concentration limits, and remediation of contaminated sites. However, with CECs as widespread as they already are, remediation of contaminated waterways is likely a losing game. It may be more effective to address these problems at the source, either by minimizing the production of certain CECs or by improving WWTP treatment technologies.

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