

News & Views

Exposure to Emerging Contaminants and Health Effects: A Stealthy Health Challenge

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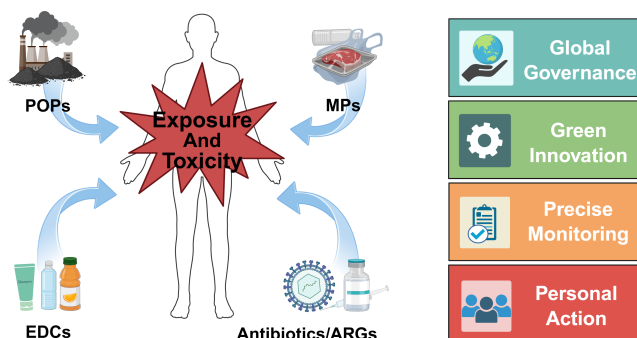
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Highlights

- ECs include four major classes: microplastics, POPs, EDCs, antibiotics and other PPCPs
- Exposure to ECs by ingestion, inhalation, dermal contact and maternal-fetal transfer
- Long-term low-dose exposure threatens endocrine, reproductive, immune systems
- Comprehensive management of ECs from source prevention to personal action

Abstract: Emerging contaminants have become a major global environmental and health challenge in the 21st century. Based on their core characteristics, they are systematically categorized into four major classes including microplastics, persistent organic pollutants, endocrine disrupting chemicals, antibiotics and other pharmaceuticals and personal care products. This article provides a detailed information on the classification, characteristics, and sources of these pollutants, highlighting their significant cross-cutting nature. It discusses the multi-pathway exposure modes through which they transfer to humans via environmental media and food chains as well as maternal-fetal transfer. Furthermore, it delves into the multiple health threats posed by long-term, low-dose exposure, including impacts on the endocrine, reproductive, developmental, and immune systems, as well as threats arising from the induction of antibiotic resistance. Finally, the article proposes strategies for building a comprehensive “source prevention-process control-end-of-pipe treatment-personal action” management framework from multiple dimensions, including global governance, green innovation, precise monitoring, and personal protection. The results enhance public awareness and provide a scientific perspective and actionable guidance for addressing this stealthy threat. This work serves as an accessible introduction and invaluable resource from a science popularization perspective for individuals at a pivotal stage in their academic or research careers, including senior-year undergraduates, new graduate students, and early-career professionals in connected fields.



1. Introduction

As we stand in the latter half of the third decade of the 21st century and reflect on the tremendous achievements made since industrialization, we must confront a severe and concomitant challenge, i.e., environmental pollution. From the initial billowing black smoke and uncontrolled wastewater discharge to later issues such as acid rain [1] and the ozone layer depletion [2], and now climate change [3], environmental problems have continuously evolved in form. Over the past two decades, a category of more concealed, complex, and potentially long-term hazardous “emerging contaminants (ECs)” has gradually been paid attention by scientists and government, becoming a new focus in the field of environment and health [4–10].

The term “emerging contaminants” was introduced in the late 20th century and early 21st century, when advances in analytical technology enabled the widespread detection of previously hard-to-identify trace pollutants in the environment, such as pharmaceuticals and personal care products (PPCPs), and endocrine disrupting chemicals (EDCs) [8,11]. Prompted by growing concern over the potential risks of these unregulated pollutants, scientists began to adopt this concept. Since then, the range of pollutants covered by this term has continued to expand. The term “emerging” in ECs does not solely refer to the novelty of their chemical structures. In fact, many so-called ECs have existed in the environment for decades. Rather, it signifies that they have been “newly recognized”, “newly detected”, and “newly assessed”. This “newness” is mainly reflected in three aspects: (1) Rapid advances in analytical technologies enable us to accurately identify these substances at extremely low concentrations, such as parts per billion (ppb) or even parts per trillion (ppt); (2) In-depth toxicological studies have revealed that even at low concentrations traditionally considered “safe”, these substances may still cause significant adverse health effects through long-term exposure; (3) Increased public environmental awareness and health concerns have driven attention and research into these potential threats, thereby promoting governance and control measures.

Based on their core characteristics in terms of environmental behavior and health effects, the wide variety of ECs can be categorized into four main categories: persistent organic pollutants (POPs) [6], endocrine disrupting chemicals (EDCs) [4], antibiotics and other PPCPs [5,10], and microplastics [7]. It is important to emphasize that these categories are not mutually exclusive; instead, there is substantial overlap and intersection among them. For example, many typical POPs, such as dioxins and polychlorinated biphenyls (PCBs), are also EDCs [4,12,13], and tetracycline belongs to the antibiotic class while also exhibiting endocrine-disrupting effects [5,14]. This intersectionality amplifies

their hazards, making risk assessment based on individual chemicals insufficient and necessitating the introduction of a “mixture effects” perspective despite this still facing significant challenges. In addition, antibiotics are often singled out from the broader category of PPCPs for separate discussion because of their heightened importance and unique environmental risks.

The risk characteristics of ECs can be summarized as “one low and three highs”: low concentration, high concealment, high exposure frequency, and high toxicity. Unlike traditional pollutants that directly stimulate human senses, they may quietly enter the human body through food, water, and air [15–18]. Long-term continuous exposure or accumulation may eventually lead to adverse health effects that manifest years later or even across generations [19–21]. This “boiling frog effect” presents unique challenges for the prevention and control of ECs.

This article will systematically outline the characteristics, sources, human exposure pathways, and health effects of these four major categories of ECs from a science popularization perspective. Drawing on international experience and practices, it will propose comprehensive prevention and control recommendations. The aim is to contribute to building an effective risk prevention system, promote collective societal action to protect the ecological environment and public health, and enhance public awareness of ECs. Additionally, to facilitate readers in tracking related research, this article prioritizes the selection of highly cited literature or review articles. The present article is particularly suitable for senior college students in related majors, graduate students who have just entered this major, and young researchers in related fields.

2. Classification and Characteristics of ECs

Similar to traditional pollutants, ECs originate from industrial production, daily life, and agricultural activities. They pose significant ecological and health risks because of their toxicity, environmental persistence, and bioaccumulative potential [22–24]. However, these chemicals have not yet been incorporated into routine environmental management, or existing regulatory measures are insufficient. In 2023, the Ministry of Ecology and Environment of China introduced the first Priority Control List of Emerging Contaminants (2023 Edition) [25], which identified 14 priority ECs.

2.1. Persistent Organic Pollutants

Persistent organic pollutants are organic compounds with specific physical and chemical properties. They collectively form a “stubborn by-product” of human technological civilization, becoming “forever chemicals” that are difficult to degrade in the environment. According to the Stockholm Convention on Persistent Organic

Pollutants (abbreviated as the Stockholm Convention) [26], POPs are defined as chemicals possessing the following characteristics: (1) High persistence: They resist photolytic, chemical, and biological degradation in the environment, with half-lives lasting for years or even decades. For instance, perfluorooctanoic acid (PFOA) can persist in the environment for decades or even over hundreds of years and has a half-life of several years in human body [27–29]; (2) High bioaccumulation: They readily transfer from environmental matrices into lipid tissues of organisms and biomagnify through food chains because of their high lipophilic and hydrophobic properties [30,31]. For example, the bioaccumulation factor for perfluorooctanesulfonate was determined to be between 6300 and 125,000, based on a comparison of its concentrations in fish liver and surface water [32]; (3) Long-range transport potential: They can undergo long-range transport via atmospheric processes like the “distillation effect” and “grasshopper effect”, as well as through water and migratory animals [33–35]. Furthermore, they have been detected in organisms in the Arctic and Antarctic, regions where they were never used [36,37]; (4) High toxicity: These substances exhibit toxic effects such as endocrine disruption, reproductive and developmental

toxicity, neurotoxicity, immunotoxicity, and teratogenic, carcinogenic, and mutagenic properties [4,20,28,38–40].

These characteristics make the pollution of POPs a truly global issue. The Stockholm Convention was signed in Sweden in May 2001 [26]. Initially, the Convention controlled 12 POPs, often referred to as the “dirty dozen”. Representative substances include intentionally produced POPs like organochlorine pesticides (OCPs), and unintentionally produced POPs like polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs). With industrial development, an increasing number of chemicals with POP-like characteristics have been identified as requiring control and added to the list, such as polybrominated diphenyl ethers (PBDEs), per- and polyfluoroalkyl substances (PFASs), and etc. [41–44]. POPs can be defined narrowly or broadly. Narrowly, they refer to the chemicals listed under the Stockholm Convention. Broadly, they include any chemicals exhibiting the properties defined by the Convention. Currently, a total of 37 (kinds) compounds are added to the list of Stockholm Convention (Table 1). It is anticipated that continued strengthening of national controls and ongoing international efforts will lead to more substances being listed under the Stockholm Convention in the future.

Table 1. List of POPs by Stockholm Convention.

Stockholm Convention Requires	Annex A	Annex B	Annex C
	Parties Must Take Measures to Eliminate the Production and Use of the Chemicals Listed	Parties Must Take Measures to Restrict the Production and Use of the Chemicals Listed	Parties Must Take Measures to Reduce the Unintentional Releases of Chemicals Listed
First batch of controlled (12) ^a (2001.5) ^b	Aldrin; Chlordane; Dieldrin; Endrin; Heptachlor; Hexachlorobenzene (HCB); Mirex; Toxaphene; Polychlorinated biphenyls (PCB)	Dichlorodiphenyltrichloroethane (DDT)	HCB; PCB; Polychlorinated dibenzo- <i>p</i> -dioxins (PCDD); Polychlorinated dibenzofurans (PCDF)
First additional listing (9) (2009.5)	Alpha hexachlorocyclohexane; Beta hexachlorocyclohexane; Hexabromobiphenyl; Chlordecone; Lindane; Pentachlorobenzene; Tetrabromodiphenyl ether and pentabromodiphenyl ether; Hexabromodiphenyl ether and heptabromodiphenyl ether	Perfluorooctane sulfonic acid (PFOS), its salts and perfluorooctane sulfonyl fluoride (PFOSF)	Pentachlorobenzene
Second additional listing (1) (2011.4)	Technical endosulfan and its related isomers		
Third additional listing (1) (2013.5)	Hexabromocyclododecane (HBCD)		
Fourth additional listing (3) (2015.5)	Hexachlorobutadiene (HCBD); Pentachlorophenol and its salts and esters; Polychlorinated naphthalenes		Polychlorinated naphthalenes
Fifth additional listing (2) (2017.5)	Decabromodiphenyl ether; Short-chain chlorinated paraffins (SCCPs)		HCBD
Sixth additional listing (2) (2019.5)	Dicofol; Perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds	Perfluorooctane sulfonic acid (PFOS), its salts and perfluorooctane sulfonyl fluoride (PFOSF)	
Seventh additional listing (1) (2021.7); (2022.6)	Perfluorohexane sulfonic acid (PFHxS), its salts and PFHxS-related compounds		
Eighth additional listing (3) (2023.5)	Dechlorane Plus; Methoxychlor; UV-328		
Ninth additional listing (3) (2025.5)	Chlorpyrifos; Long-chain perfluorocarboxylic acids, their salts and related compounds; Medium-chain chlorinated paraffins (MCCPs)		

Note: the information from web site: <https://www.pops.int/TheConvention/ThePOPs/AllPOPs/tabid/2509/Default.aspx> (accessed on 17 November 2025); ^a: number of the compounds; ^b: time of the files.

2.2. Endocrine Disrupting Chemicals

Environmental EDCs are exogenous substances that can interfere with the normal functions of the endocrine system and induce adverse health effects in an organism or its progeny [4]. The endocrine system is a precise network regulating growth, development, metabolism, reproduction, and behavior. Representative environmental EDCs include bisphenol A (BPA) and its alternatives, phthalate acid esters (PAEs), many PPCPs and POPs which have been confirmed as potent EDCs, exemplifying the cross-cutting nature of this classification [38,45–47].

Endocrine disrupting chemicals can disrupt endocrine system through various mechanisms, acting as “mimics” within the hormonal system. Examples of mechanisms include: (1) Mimicking natural hormones (e.g., BPA mimics estrogen by binding to estrogen receptors, triggering excessive responses); (2) Blocking hormone receptors, preventing natural hormones from binding and thus inhibiting their normal function; (3) Interfering with the synthesis, metabolism, or transport of hormones, affecting their concentration and availability; and (4) Epigenetic regulation (e.g., via DNA methylation, histone modification), potentially leading to transgenerational effects on gene expression [19,48–51].

2.3. Antibiotics and Other PPCPs

Pharmaceuticals and personal care products, a term first introduced by Daughton and Ternes [11], refer to a wide range of substances used by humans and animals, including pharmaceuticals (such as antibiotics, analgesics, and hormones) and active ingredients in personal care products (such as cosmetics, fragrances, and sunscreens). With the rapid development of the pharmaceutical and personal care industries, the global production and usage of PPCPs have continued to increase [52]. These compounds enter the environment through pathways such as domestic wastewater, and improper disposal, and have been widely detected in various environmental matrices including air, water bodies, soil, sediment, and so on. Their concentrations in water typically range from nanograms to micrograms per liter, with some even reaching milligrams per liter levels. For example, compounds like diclofenac (analgesic) reached a concentration of 1.3 mg L⁻¹ in the aquifer systems of Delhi, India [52]. PPCPs are often persistent and not fully degradable, and some possess biological activity and may cause endocrine disruption in aquatic organisms, promote bacterial antibiotic resistance, and pose potential risks to human health through drinking water or food chains. Consequently, the health risks and control strategies associated with PPCPs have become an important research focus in environmental science and public health. Among PPCPs, antibiotics are frequently singled out for separate discussion in scientific research because of their extreme importance and distinct

environmental risks. This article will provide a brief introduction to these substances.

Antibiotics are chemicals capable of inhibiting bacterial growth or killing bacteria, hailed as one of the greatest medical discoveries of the 20th century. The development of antibiotics can be traced back to the discovery of penicillin by Alexander Fleming [53], followed by chemists discovering sulfonamides in 1935 [54]. Antibiotics primarily include therapeutic drugs commonly used in humans and animals. They can be classified into various categories based on their chemical structure or mechanism of action (Figure 1), such as sulfonamides, quinolones, tetracyclines, macrolides, chloramphenicols, β -lactams, and aminoglycosides. Among these, the latter four are the most widely used antibiotics, often referred to as the “Big Four” [55]. They primarily function through four main mechanisms (Figure 2). For instance, β -lactams (e.g., penicillin) disrupt bacterial cell wall synthesis [56]; tetracyclines and aminoglycosides inhibit bacterial protein synthesis [57,58]; fluoroquinolones (e.g., ciprofloxacin) kill bacteria by interfering with DNA replication [59]; and sulfonamides competitively inhibit bacterial folate metabolism [60]. These drugs play an irreplaceable role in treating bacterial infectious diseases in humans and animals.

Although there are reports warns that without effective measures, antibiotic resistance could cause 10 million deaths annually by 2050, surpassing cancer deaths [61,62]. The abuse of antibiotics not only lead to the residual presence of the drugs themselves in the environment but, more alarmingly, strongly select for and promote the emergence and spread of antibiotic resistance genes (ARGs) [63,64]. ARGs are genetic fragments carried by bacteria that enable them to resist the effects of antibiotics. These ARGs can spread among different bacteria via horizontal gene transfer, facilitating the exchange of resistance between the environment, animals, and humans [63,65]. This ultimately forms a shared “resistome” accessible to diverse bacteria, significantly increasing the difficulty of treating infectious diseases and posing a severe threat to global public health security [66]. ARGs are considered a novel type of “genetic pollutant”, drivers of “superbugs”, and contributors to the spread of resistance [15,67]. Their hazard is more severe and persistent than antibiotic residues alone. Therefore, ARGs are often considered as ECs and discussed alongside antibiotics.

Antibiotics in the environment primarily originate from the following sources [66,68,69]: (1) Domestic sewage discharge: Patient excreta contain unmetabolized antibiotics and their metabolites. Because of incomplete bioavailability, approximately 50–80% of administered antibiotics are excreted in feces and urine as the parent drug or its metabolites, thereby entering wastewater treatment plants; (2) Medical wastewater: Hospital sewage and pharmaceutical industrial wastewater are two major sources of environmental antibiotic pollution. The former originates from hospital sewage, while the

latter contains effluent from manufacturing processes with high concentrations of antibiotics; (3) Livestock, aquaculture and agriculture: Antibiotics are extensively used in livestock and aquaculture for therapy, prevention,

and growth promotion. In addition, their residues and resistance genes are then introduced into soils and crops via irrigation with manure-based fertilizers, creating a major dissemination pathway.



Figure 1. Classification of antibiotics and some representative substances.

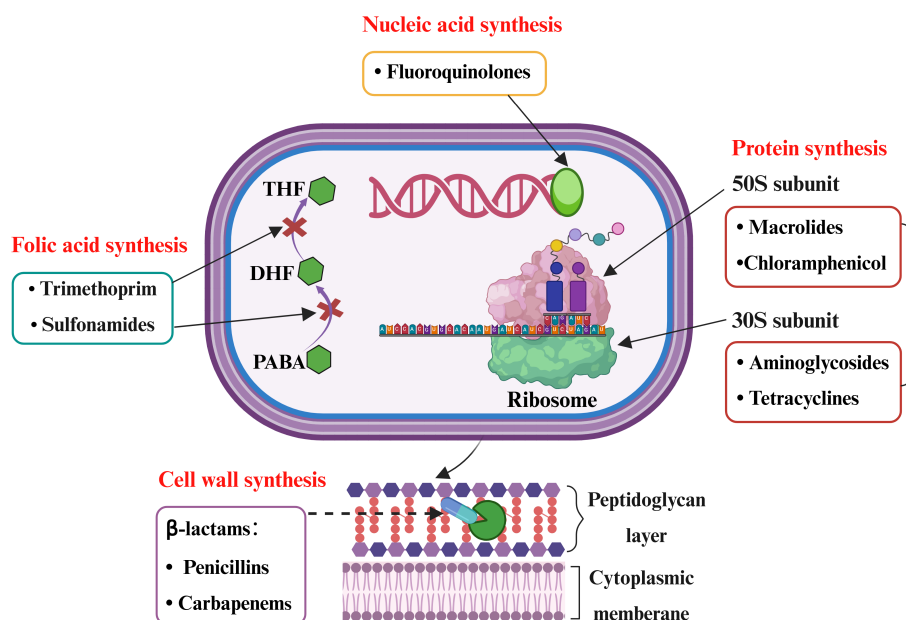


Figure 2. Four action mechanisms of antibiotics (PABA: para-aminobenzoic acid; DHF: dihydrofolic acid; THF: tetrahydrofolic acid).

2.4. Microplastics

Environmental microplastic pollution was first identified in surface waters in 1972 [70]. The concept of microplastics was first proposed by Thompson et al. [71].

Since then, microplastics have been widely detected in ecosystems including the atmosphere, pedosphere, hydrosphere, urban sewage treatment systems, as well as in table salt, drinking water, food, and biological samples

(including humans), raising increasing concerns about their potential risks to ecological environment and human health [16,72–75]. A meeting organized by the US National Oceanic and Atmospheric Administration in 2008 proposed 5 mm as the upper size limit for microplastics, which remains the most widely used size definition today [76,77]. However, with increasing research and varying separation and detection methods, there is currently no consensus on the lower size limit because the lower size bound is generally limited by the capabilities of available methods to isolate and identify particles within complex environmental mixtures. Therefore, microplastics are now commonly defined as plastic particles or fragments with a particle size of less than 5 mm, which is accepted and recognized by most scholars [77]. Furthermore, some scholars suggest subdividing microplastics into two types: 1 μm –5 mm and <1 μm , with the latter termed nanoplastics, or further subdivided into sub-micron plastics (100–1000 nm) and nanoplastics (1–100 nm) [78].

Microplastics can be categorized into primary and secondary microplastics [77,79]. Primary microplastics are manufactured directly as small particles, such as microbeads in cosmetics, toothpaste, and industrial abrasives. These microplastics are being gradually phased out as they are easier to identify and regulate. Secondary microplastics result from the fragmentation of larger plastic waste (e.g., plastic bags, bottles, fishing nets, tire wear) in the environment through weathering, ultraviolet

radiation, and mechanical abrasion. They constitute the main source of microplastics in the environment. The hazard of microplastics lies not only in their physical damage and leaching of chemical additives (e.g., EDCs) but also in their role as ubiquitous adsorption carrier for other toxic pollutants (e.g., POPs) [78,80,81]. Currently, microplastics have been detected in the most remote parts of the planet, from the sediments of the Mariana Trench to snow samples on Mount Everest [82,83], and from Arctic sea ice to urban air [84,85], suggesting the ubiquitous occurrences of the toxic particles in the environment.

3. Human Exposure Pathways

Emerging contaminants have established a global exposure network, entering the human body through multiple pathways and forming silent channels of invasion [86] (Figure 3). These pollutants are so pervasive that humanity has virtually no refuge. Understanding the pathways of the pollutants exposure to humans is fundamental for risk assessment and the design of interventions. It should be noted that this article primarily demonstrates to readers the sources and pathways through which these ECs enter the human bodies and cause health risk. Because of their physicochemical properties, the main sources and exposure pathways of different ECs may vary significantly.

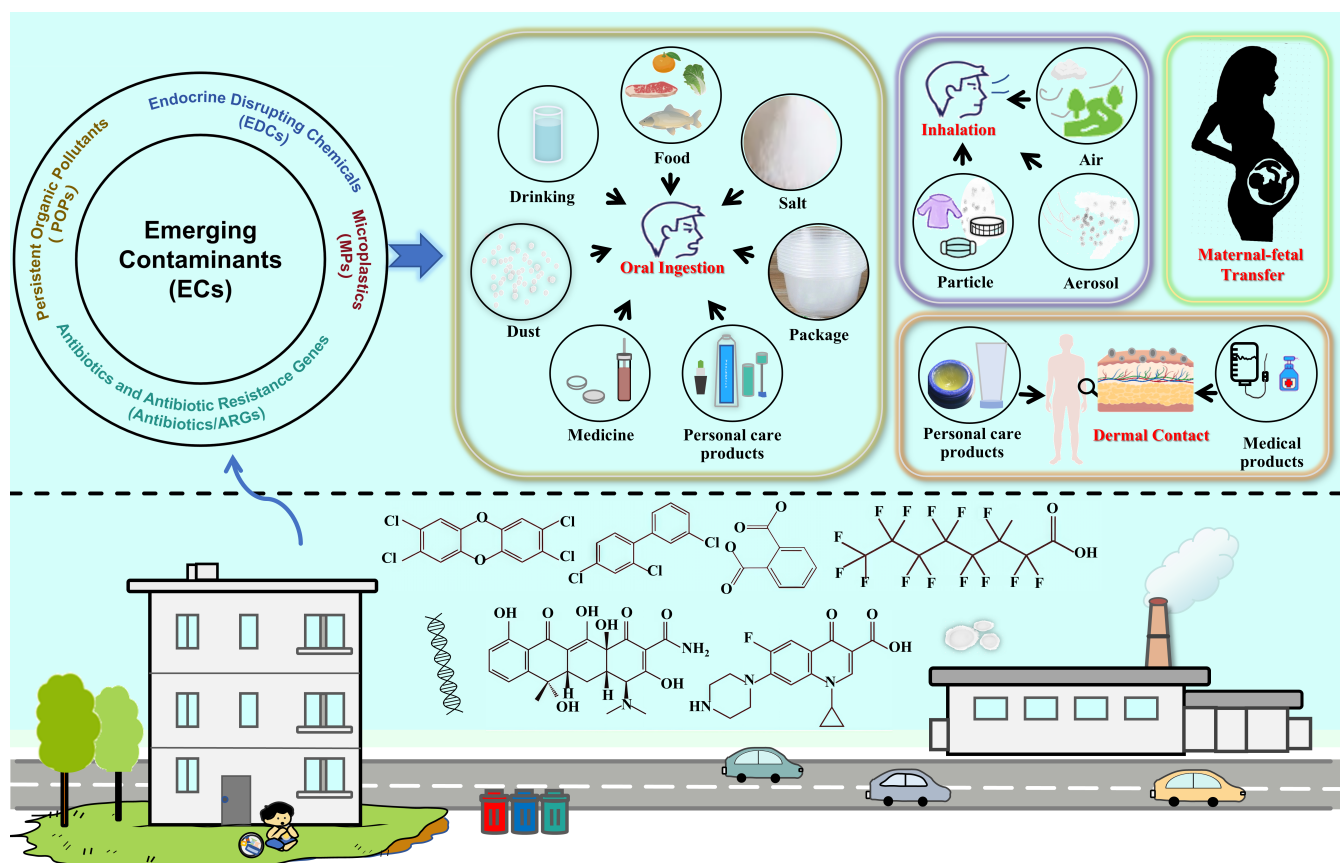


Figure 3. Sources and pathways of human exposure to emerging contaminants.

3.1. Oral Ingestion

Oral ingestion is one of the primary pathways for human exposure to ECs, primarily originating from water, diet and soil/dust ingestion. For POPs, they bioaccumulate and biomagnify, leading to high concentrations in the fatty tissues of fish, shellfish, meat, and thus exposure to human by food [87]. Moreover, substances (e.g., BPA and PAEs) can migrate from plastic packaging into food (especially under acidic or high-temperature conditions) [88,89]. A study found that $646.5 \mu\text{g kg}^{-1}$ BPA can migrate into food from an organosol coating of tuna fish cans [89]. Wastewater irrigation and the application of organic fertilizers containing ARGs present a potential route for human exposure through crop uptake of contaminants, although the findings across studies are variable [90,91]. A comprehensive understanding and effective management of ARG transfer through the food chain from agricultural ecosystems to humans are imperative, warranting further investigation.

Water is an important source of many ECs, particularly hydrophilic compounds and microplastics. Currently, conventional water treatment processes (coagulation, sedimentation, filtration, and disinfection) struggle to completely remove PFASs, various pharmaceutical residues, and nanoplastics [17,23,61,92,93]. Bottled water is not immune, and these ECs are ingested through drinking water. A study by Zhang et al. showed that the concentration of microplastics in bottled drinking water were approximately 10^8 particles/mL and the annual human intake was estimated to be about 10^{14} particles [94].

3.2. Inhalation

Human survival is intricately linked to the atmosphere, with each person inhaling an average of $14.5\text{--}18.1 \text{ m}^3$ of air each day for an adult. Residents inhale varying amounts of fine particulate matter ($\text{PM}_{2.5}$) daily, dependent on location and air quality. A study estimated that the maximum annual exposure to airborne microplastics for humans in Chinese megacities is in the range of 1–2 million [95]. Airborne microplastics and $\text{PM}_{2.5}$, and dust (especially household dust containing flame retardants and plasticizers released from electronics and furniture) that have adsorbed POPs/EDCs can be inhaled directly into the alveoli and potentially enter the bloodstream [96–98]. In addition, some semi-volatile POPs/EDCs and other substances in gaseous phase can be inhaled directly into the alveoli and be absorbed [97,99]. For instance, gaseous PCDD/Fs accounted for approximately 30% of the totals in air, and the estimated daily intake of PCDD/Fs for park workers via inhalation ranged from 0.099 to $0.227 \text{ pg I-TEQ kg}^{-1} \text{ day}^{-1}$ [99].

3.3. Dermal Contact

The skin is the largest organ of the human body, possessing a significant absorptive function. POPs, PAEs,

BPA, and many chemicals can be absorbed in significant amounts directly through the skin, although the skin barrier is relatively effective [100,101]. As reported by Liao and Kannan [100], the transfer of BPA from thermal receipt paper to currencies was found to be a significant source of exposure, with dermal absorption during daily handling estimated to result in an intake on the order of a few nanograms per day. Furthermore, a significant increase in post-shift urinary BPA levels was observed among 31 cashiers who handled BPA-containing receipts relative to non-cashiers [102]. Through controlled chamber exposure experiments with human participants and biomonitoring of urinary metabolites, Weschler et al. demonstrated that diethyl phthalate (DEP) and di(*n*-butyl) phthalate (DnBP) can directly enter the human body via dermal absorption from air [103]. In addition, studies using hand wipes have detected numerous chemicals, including PFASs, PBDEs, OPFRs, and polycyclic aromatic hydrocarbons (PAHs), on skin surfaces, confirming dermal exposure potential [104–107]. In addition to organic compounds, there are evidence that microplastics can also be absorbed into the human body through the skin, especially for particles smaller than 100 nm [108]. More research is needed in this field, especially since microplastics often adsorb various toxic substances.

3.4 Maternal-Fetal Transfer

For the fetus, maternal-fetal transfer represents the most significant route of exposure to ECs. The vast majority of POPs (e.g., PBDEs, PCBs, and PFASs), EDCs (e.g., BPA and PAEs), and antibiotics, and even microplastics can cross the placental barrier, directly affecting the developing fetus [21,109–111]. Research has detected up to 287 industrial chemicals in newborn umbilical cord blood, including known carcinogens, neurotoxicants, and endocrine disruptors (<https://ecocrap.wordpress.com/tag/pregnancy/> (accessed on 17 November 2025)), although the placental transfer ratios of the chemicals were compound-specific. For example, the placental transfer ratios BPA, bisphenol AF, and bisphenol S were 1.94, 3.26, and 1.11 [111], while PBDEs were approximately 0.46 [112]. In addition, compelling evidence indicates that microplastics can transfer from the mother to the developing offspring [113]. For the first time, microplastic fragments have been detected in human placentas from patients with normal pregnancies [114]. The early life stages (embryo, fetus) represent the most critical window of development for all body systems, a period of extreme vulnerability and sensitivity to external disturbances. Exposure during this time can cause irreversible lifelong effects. Therefore, much more study should be conducted in the field in the future.

3.5. Challenges in Exposure Assessment

Exposure assessment for ECs faces multiple challenges. Firstly, the vast number of chemical species, with new compounds continually being synthesized and used. Secondly, the complexity of exposure pathways, with multiple routes potentially contributing simultaneously to the total exposure. Thirdly, significant individual variability, where factors like age, gender, dietary habits, occupation, and geographical location influence actual exposure levels. Meanwhile, it must be noted that regardless of the pathway through which these pollutants enter the human body, they are not fully absorbed. In health risk assessment, absorption efficiency (generally represented by bioavailability or bioaccessibility) is a critical factor. This efficiency is significantly influenced by the matrices, the properties of

pollutants, and the pathways of human exposure. Fourthly, a lack of standardized monitoring methods of the pollutants in the environment matrices and the detection methods of the absorption efficiency, as well as databases for them. Therefore, developing exposomics approaches based on biomonitoring and computational models will be an important direction in the future.

4. Exposure Effects

The core health risk of ECs lies in their characteristics of “low-dose, long-term, mixture exposure”. Their health effects are often chronic, latent, and interfere with life processes at the molecular level, ultimately manifesting as various chronic adverse effects and functional disorders, which is a systemic assault from long-term, low-dose exposure (Figure 4).

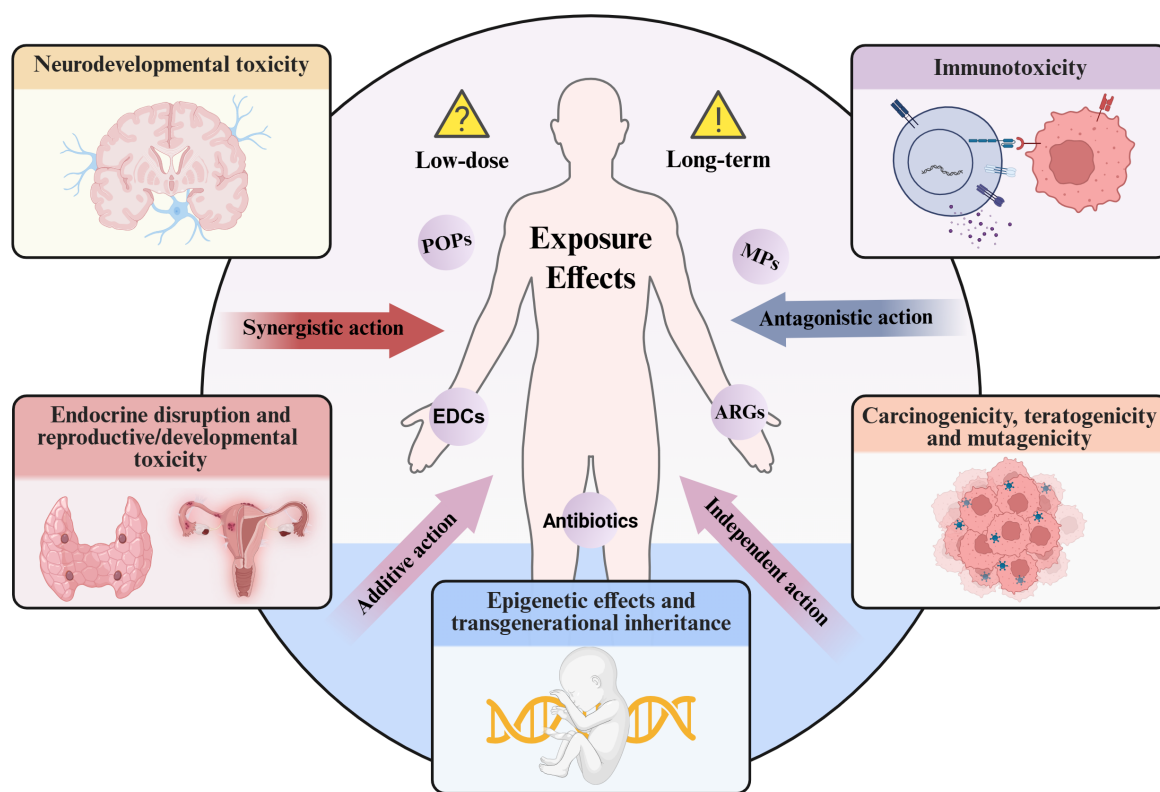


Figure 4. Exposure effects of emerging contaminants in human body.

4.1. Endocrine Disruption and Reproductive/Developmental Toxicity

Global data show a decline of sperm count over 50% during 1930s–1990s [115]. The endocrine disruption and reproductive/developmental toxicity of ECs are primarily driven by POPs/EDCs. These pollutants can lead to declining sperm counts deteriorated sperm quality, increased risk of testicular cancer, and cryptorchidism [45,116,117]. The global deterioration of male reproductive health indicators is highly correlated with EDC exposure [118,119]. In females, these substances are associated with early puberty (age of puberty onset in girls has significantly

advanced over the past decades), polycystic ovary syndrome, endometriosis, premature ovarian insufficiency, and increased breast cancer risk [120–123].

The developmental toxicity of POPs/EDCs can manifest as effects on fetal programming from prenatal exposure, leading to birth defects, low birth weight, and neurodevelopmental delays [124,125]. A large-scale meta-analysis revealed a statistically significant association, with each 1- $\mu\text{g}/\text{L}$ increase in cord serum PCB153 (a PCB congener) corresponding to an adjusted birth weight decline of 150 g (95% CI: -250 g, -50 g) [126]. In addition, metabolic disorder-related diseases can be mediated by EDCs, which disrupt the endocrine system and contribute

to their pathogenesis. POPs/EDCs are strongly linked to obesity (environmental obesogens), type 2 diabetes, and thyroid dysfunction [127,128]. Therefore, endocrine disruption serves as a unifying mechanism through which many ECs exert profound and interlinked toxicities on both the reproductive and developmental processes.

4.2. Neurodevelopmental Toxicity

The developing brain is a prime target for EDCs. The fetus and infant, whose blood-brain barrier is not fully formed, are particularly vulnerable. Prenatal and childhood exposure to ECs is significantly associated with childhood attention-deficit/hyperactivity disorder, autism spectrum disorder, impaired learning and memory ability, and decreased intelligence quotient [129–131]. A study confirms that exposure to PAEs leads to an eight-fold increase in the visual Advanced Test of Attention commission error T-score among children diagnosed with attention-deficit/hyperactivity disorder [131]. There are evidence that antibiotics (such as tetracyclines) and microplastics can cause neurodevelopmental toxicity [9,132]. Furthermore, emerging substitutes, notably bisphenol AF among bisphenol analogues and hexafluoropropylene-oxide-dimer-acid among PFASs, exhibit more significant neurodevelopmental toxicity as reviewed by Morales-Grahl et al. [130]. Future research on the developmental toxicity of next-generation pollutants is critically important to prevent the replacement of known hazardous chemicals with equally or more harmful alternatives, thereby informing evidence-based regulatory policies.

4.3. Immunotoxicity

Immunotoxicity refers to the adverse effects on immune function caused by exogenous substances. In 2020, the European Food Safety Authority (EFSA) identified impaired immune function as the most serious concern for human health risk assessment, citing evidence from diminished childhood vaccine antibody responses and corroborating findings in animal studies [133]. Evidence indicates that exposure to POPs, EDCs, antibiotics, and microplastics can induce immunosuppression, compromise vaccine efficacy, and elevate the risk of infection [133–135]. For instance, trimethoprim was immunotoxic at 20 mg/L whereas erythromycin elicited same detrimental effects at higher concentrations on *Mytilus edulis* [135].

These ECs can also cause immune dysregulation, promoting allergies, asthma, and autoimmune diseases [136–138]. For example, through integrated analysis on EDCs including PAEs, bisphenols, some PPCPs (e.g., parabens, triclosan, and benzophenone-3), Casas and Gascon [138] concludes that the EDCs collectively disrupt immune homeostasis by altering airway and gut barrier integrity, skewing T-cell responses towards a

T(H)2/T(H)17 profile while impairing Treg function and innate immunity. From a mechanistic perspective, these ECs generally can disrupt the immune response by mechanisms such as aberrant recruitment of innate immune cells (e.g., macrophages and neutrophils) and dysregulated release of inflammatory cytokines (e.g., IL-1 β and TNF- α), ultimately leading to impaired host defense or tissue damage [134].

4.4. Epigenetic Effects and Transgenerational Inheritance

Of particular concern is that ECs (especially EDCs) may exert effects through epigenetic mechanisms (e.g., DNA methylation, histone modification), and these effects can potentially span generations [19,139]. Animal experiments have shown that prenatal exposure to certain EDCs (e.g., PCBs) can cause body weight and hormonal effects in offspring, an effect that can persist for 3 generations [20]. Epigenetic effects were also observed for microplastics. For example, a study using *Daphnia magna* demonstrates that microplastics induce epigenetic effects, exemplified by global DNA hypomethylation and subsequent dysregulation of key genes such as the downregulation of Vitellogenin 1 [140]. These results suggest the health impacts of ECs may be far more profound than previously understood.

4.5. Carcinogenicity, Teratogenicity, And Mutagenicity

Carcinogenicity and teratogenicity refer to the ability of a substance to cause cancer or to increase its incidence and to cause birth defects or developmental abnormalities in an embryo or fetus, respectively, while mutagenicity refers to the ability of a physical or chemical agent (a mutagen) to cause mutations in the genetic material (e.g., DNA) of an organism. Mutagenicity can lead to carcinogenicity. However, teratogenicity is distinct. It specifically affects prenatal development and is not primarily about causing cancer or permanent genetic changes in the parent. The International Agency for Research on Cancer has classified some ECs as carcinogens or agents with sufficient or limited evidence in humans [141]. For instance, 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is classified as Group 1 (carcinogenic to humans), linked to increased risk of various cancers, and PFOA is classified as Group 2B (possibly carcinogenic to humans), strongly linked to kidney and testicular cancer. More information can be found in the literature cited above.

4.6. Antibiotic Resistance Genes

Antibiotic resistance genes is the most critical health threat posed by antibiotics as ECs. ARGs in the environment are transferred to human pathogens via food, water, etc., leading to drug-resistant infections, which is a unique “indirect” health effect [15,68,142]. This means conventional antibiotic treatments fail, leading to prolonged illness, increasing mortality risk, and sharply

rising healthcare costs. In the United States alone, there are approximately 2.8 million antimicrobial-resistant infections annually [143]. In 2020, the World Health Organization has declared ARGs is one of the top 13 global public health challenges for the next decade [144].

4.7. Mixture Toxic Effects

In the real-world scenarios, humans are simultaneously exposed to mixtures of hundreds of low-concentration ECs. Using a specific toxicity endpoint as an observation indicator, these substances can produce four main combined effects:

Additive action: $M = M_1 + M_2$

Synergistic action: $M > M_1 + M_2$ (most concerning)

Antagonistic action: $M < M_1 + M_2$

Independent action: $M = M_1 + M_2 (1 - M_1)$

where M_1 and M_2 are the effects of two individual chemicals, and M is the combined effect. For example, an evaluation using the embryonic stem cell test showed that the combined effects of PFOA with perfluorooctane sulfonic acid (PFOS) or BPA were additive; in contrast, the PFOS and BPA combination acted synergistically on myocardial differentiation [145]. Reports of antagonism among pollutants like EDCs, POPs, and microplastics are very limited. They are more frequent between antibiotics and drugs, as demonstrated by the antagonistic action between 1,4-naphthoquinone and cefuroxime against methicillin-resistant *Staphylococcus aureus* strains [146], and antagonistic action between erythromycin and spiramycin in clinical isolates [147]. Relatively, researches on independent effects have received relatively less attention [148,149], while synergistic action is the most concerning combined effect.

It is crucial to note that the classification of ECs is not isolated, and cross-cutting characteristics are a core feature. “POPs + EDCs”: Dioxins, PCBs, PBDEs, etc., are typical “dual-threat” substances possessing both persistence and endocrine-disrupting properties. Research shows PBDEs not only persist and bioaccumulate but also disrupt normal thyroid, estrogen, and androgen function [150–152]. “Microplastics + POPs/EDCs”: Microplastics themselves may contain additives (e.g., PAEs), and their porous surfaces can efficiently adsorb environmental POPs/EDCs, acting as their “vector”, greatly increasing the bioavailability of contaminants [80,81]. “Antibiotics + ARGs”: Antibiotic residues exert direct selection pressure, promoting the spread and proliferation of ARGs, while ARGs themselves can persist and spread in different environmental media [66].

This interdisciplinary characteristic implies that real-world exposure invariably involves complex mixtures of multiple toxic substances, whose combined health risks substantially exceed the additive effects of individual compounds. The existing chemical risk assessment and management framework, which is predominantly based on

single-substance evaluation, is insufficient to address this complexity. There is therefore a pressing need to develop new assessment approaches that incorporate mixture toxicity. The current regulatory paradigm relying on “safe thresholds” for individual chemicals cannot accurately reflect the actual risks posed by such combined exposures, representing a major methodological gap and one of the most significant challenges in contemporary environmental health risk assessment. Indeed, the mixture effects of pollutants is one of the greatest scientific challenges currently facing toxicology.

5. Strategies for Building a Full-Chain Prevention and Control System

Addressing the challenge of ECs requires an integrated prevention and control strategy encompassing “source prevention, process reduction, end-of-pipe treatment, and risk management”, necessitating the participation of governments, enterprises, research institutions, and the public.

5.1. National and Global Governance

Governments need to start with top-level design, improving laws, regulations, and standard systems, and incorporating more ECs into priority control lists. Stricter environmental quality standards, emission standards, and limits for hazardous substances in products must be established. For instance, China’s 2022 Action Plan for the Management of Emerging Contaminants marks the formal inclusion of these pollutants into the national agenda [153]. To strengthen national and global governance of ECs, we need to: (1) Strengthen international convention implementation, and strictly enforce international conventions like the Stockholm Convention (for POPs) to reduce and eliminate the production and use of controlled chemicals; (2) Establish national monitoring and assessment networks, conducting nationwide environmental surveillance and human biomonitoring for ECs to dynamically assess population exposure levels and health risks, enabling targeted management. Programs like the US CDC’s National Report on Human Exposure to Environmental Chemicals (<https://www.cdc.gov/environmental-exposure-report/index.html> (accessed on 17 November 2025)), and the European Human Biomonitoring Initiative (HBM4EU) provide excellent models (<https://www.hbm4eu.eu/about-us/about-hbm4eu/> (accessed on 17 November 2025)); (3) Implement green taxes and extended producer responsibility. Levy environmental taxes on products containing hazardous chemicals and implement extended producer responsibility systems, compelling enterprises to consider the environmental impact of their products throughout their entire life cycle from the design phase. The European Union Chemicals Strategy for Sustainability,

while still a work in progress [154], offers valuable insights for global reference.

5.2. Technological Innovation and Industrial Transformation

Enterprises and research institutions must drive the continuous iterative upgrade of products and green technologies. This process is the core driver of technological innovation and industrial transformation. The chemical industry must invest in research and development to provide non-toxic or low-toxic alternatives to POPs/EDCs (e.g., novel green flame retardants, plasticizers, fluorine-free water repellents), and conduct safety assessments of alternatives to avoid “regrettable substitution”. Enterprise needs upgrade wastewater and solid waste treatment technologies, promotes the application of advanced treatment processes like membrane bioreactors in wastewater treatment plants to enhance the removal efficiency of ECs, and develops highly efficient dioxin control technologies for waste incineration plants and specialized treatment technologies for wastewater from hospitals and pharmaceutical factories. Furthermore, they should develop circular economy and eco-design, avoiding using hazardous substances from the product design stage, extending product lifespan, and improving recyclability to fundamentally reduce waste and pollution, promoting closed-loop recycling of plastics and the development of sustainable alternative materials. In addition, we should regulate the usage of antibiotics, strictly implement prescription management, and reduce antibiotic use in healthcare and animal husbandry to curb the environmental discharge of antibiotics and ARGs at the source.

5.3. Public Awareness and Individual Action

To protect our health and environment, we should make informed consumer choices by reducing plastic use. This includes using reusable cups and bags, refusing single-use plastics, and choosing personal care products without microplastic abrasives. We should also avoid heating food in plastic containers, minimize consumption of plastic-packaged foods, and prefer glass or stainless-steel tableware and water bottles. It is crucial to check plastic recycling codes and avoid types 3 (PVC, which may contain PAEs), 6 (PS, which may contain styrene), and 7 (which may contain BPA). Additionally, we ought to choose personal care products and cosmetics that are explicitly labeled “Phthalate-Free”, “BPA-Free”, or “Paraben-Free”.

To ensure home health, we can take actions such as installing certified effective home water filters like reverse osmosis systems and replacing the filters regularly. We should dust frequently with a damp cloth and use efficient air filters to reduce exposure to flame retardants and plasticizers that accumulate in household dust. Maintaining good indoor ventilation is also important to reduce

concentrations of ECs. Furthermore, we must never flush expired medications down the toilet or drain but instead return them to designated pharmacies or community hazardous waste collection points.

For diversifying risk and advocacy, we are advised to diversify our diets to avoid overconsuming any single type of potentially highly contaminated food, such as certain large predatory fish, and can refer to local food safety guides for aquatic products. We should also enhance our personal awareness, support environmental organizations, and express our concerns to policymakers to advocate for stricter chemical management policies. Finally, we can participate in community environmental activities, disseminate scientific knowledge, and become active advocates for environmental protection and healthy living.

6. Conclusions and Perspective

This article outlines the characteristics, sources, human exposure pathways, and health effects of the four main ECs from a science popularization perspective. ECs represent a complex and tricky challenge embedded within the process of modernization. With their characteristics of persistence, bioaccumulation, toxicity, cross-cutting nature, and mixture exposure, they pose profound, potential, and irreversible threats to the global environment and human health. We face not only known substances but also countless “unknown unknowns” yet to be identified and assessed. Facing this challenge, scientific understanding continues to deepen. Future research needs to: (1) Develop more sensitive and efficient analytical methods to identify more ECs and their transformation products in environmental and biological samples; (2) Deepen the understanding of the health effect mechanisms of low-dose mixture exposure, breaking through the risk assessment bottleneck of the “cocktail effect”; (3) Conduct large-scale, long-term cohort studies to establish causal links between environmental exposure and specific diseases; (4) Accelerate the research and application of green alternative materials to eliminate pollution at the source; and (5) explore intervention and detoxification strategies, such as developing nutritional or medical interventions that promote the excretion of contaminants.

It is widely acknowledged that solving the problem of ECs cannot rely on a single technology or policy. It requires a profound systemic transformation, i.e., shifting from a linear to a circular economy, from end-of-pipe treatment to source prevention, and from government-led action to societal synergy. This demands the joint efforts of scientists, policymakers, entrepreneur, and the public to build a new paradigm based on the precautionary principle and ecosystem health. Each of us is not only a potential victim of pollution but also a potential part of the solution. We can hope to weave a

cleaner, safer future for current and future generations by the combined power of scientific knowledge, policy action, and citizen choices. The challenge of ECs, though formidable, is not insurmountable. Facing the invisible threat of ECs, we must reclaim this capacity to foresee and forestall, striving for a more sustainable future.

Author Contributions

Y.Z. (Yinfeng Zhou): writing, data analysis; X.Y.: writing, data analysis; Y.Z. (Yuan Zhang): data collection; J.O.: data collection; Y.X.: data analysis; Y.Y.: Review & editing, design. All authors have read and agreed to the published version of the manuscript.

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The authors declare no conflict of interest.

Use of AI and AI-assisted Technologies

Subsequent to the completion of the manuscript, the text was polished for language with the assistance of Deepseek, an AI-driven tool. The authors are solely and entirely responsible for the published content.

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