

Neuroendocrine disruptors and micro-nanoplastics in low-resource settings: emerging threats to environmental and human health

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Abstract

Neuroendocrine Disruptors (NEDs) are increasingly recognized as a significant environmental and public health concern, particularly in low-resource settings where environmental contamination and inadequate waste management may increase human exposure. NEDs include a heterogeneous group of exogenous chemicals capable of interfering with hormonal and neurotransmitter systems, thereby altering neuroendocrine regulation and potentially affecting multiple physiological processes. This review examines the main sources of exposure to NEDs in populations living in low-resource environments, with particular attention to micro- and nanoplastics, pesticides, bisphenols, phthalates, and dioxins. Evidence from experimental and epidemiological studies indicates that these contaminants may influence neurodevelopment, reproductive health, metabolic regulation, and immune function. Vulnerable populations – including pregnant women, fetuses, children, and occupationally exposed workers – appear particularly susceptible to the effects of NED exposure. In addition, environmental pathways such as contaminated water, food products, cosmetics, and electronic waste represent important routes of human exposure, especially in regions characterized by rapid industrialization and limited regulatory oversight. The review also discusses the challenges faced by low- and middle-income countries in monitoring and mitigating exposure to neuroendocrine disruptors. Finally, emerging strategies aimed at reducing environmental contamination are explored, including improved waste management policies, preventive public health measures, and the potential application of artificial intelligence technologies for the rapid detection of nano-microplastics in consumer products. Strengthening research capacity and environmental health policies in low-resource settings is essential to reduce exposure and protect vulnerable populations.

Key words: micro- and nanoplastics, pesticides, environmental pollution, neuroendocrine disruptors, neuro development.

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Introduction

Human exposure to Micro- and Nanoplastics (MNPs) represents a global challenge due to their widespread presence in the environment. However, significant knowledge gaps remain regarding their adverse effects on organs and tissues, including the endocrine system.¹ Neuroendocrine Disruptors (NEDs) represent an underestimated public health challenge worldwide, with a higher risk in low-resource settings.² NEDs are a group of exogenous substances that mimic, block, or interfere with hormones and neurotransmitter functions, acting as agonists or antagonists of hormone receptors and leading to dysregulation of the neuroendocrine system.^{3,4} NEDs are ubiquitous in environmental, industrial, and agricultural contexts, with high levels of contamination in developing nations characterized by heavy pesticide reliance, weak regulatory oversight, and limited waste management.⁵ The major sources of exposure to NEDs are industrial and electronic waste,

agricultural pesticides, water contamination, consumer goods and plastics. MNPs, defined as plastic fragments smaller than 5 mm, have recently been identified as endocrine disruptors, mainly due to the chemicals they release.⁶ MNPs have been reported to disrupt the Hypothalamic-Pituitary-Gonadal (HPG), Hypothalamic-Pituitary-Thyroid (HPT), and Hypothalamic-Pituitary-Adrenal (HPA) axes, with potential short- and long-term effects on endocrine glands and overall human health.⁷ Endocrine disruption induced by MNPs occurs through the aberrant activation or inhibition of signaling pathways that interfere with hormonal balance and trigger apoptosis, oxidative stress, and inflammation in endocrine cells.⁸ Due to their small size (microplastics < 5 mm; nanoplastics < 1 µm), MNPs can cross the intestinal and respiratory barriers, enter the bloodstream, and affect the function of various body systems, including the digestive, reproductive, and nervous systems, by inducing cellular stress such as oxidative stress and endoplasmic reticulum stress.⁹ Furthermore, due to widespread

plastic pollution in soil, rivers, and oceans, MNPs can affect a wide range of organisms, including terrestrial and marine invertebrates and vertebrates. This leads to the amplification of toxic effects along the food chain, ultimately posing risks to human reproductive health.¹⁰ MNPs have been shown to accumulate in the heart, promoting the development of acute and chronic cardiac pathologies, including abnormal heart rate, impaired cardiac function, and myocardial fibrosis. This suggests that MNP exposure may represent a novel cardiovascular risk factor.¹¹

Taken together, these data clearly demonstrate that plastic pollution resulting from human activities represents a critical global threat to human health, with MNPs playing a key role due to their ability to enter human cells and act as endocrine disruptors.

The aim of this work is to provide the most recent literature regarding the major sources of exposure to NEDs in populations living in low-resource settings, with particular focus on high-risk populations and vulnerable subjects. We also discuss the neuroendocrine health impacts of NEDs, with special attention to neurodevelopmental disorders. The work's purpose is to highlight the key role of MNPs as potential toxicants and endocrine disruptor. The final sections of this review focus on the challenges faced by low-resource nations and on potential mitigation strategies aimed at improving the protection of exposed populations from the detrimental effects of MNPs and NEDs. The possible role of artificial intelligence (AI) models in addressing this challenge is also discussed.

Search and selection methodology

An integrative literature review was conducted using peer-reviewed articles published between 2020 and 2025, retrieved from databases such as PubMed, Scopus, and ScienceDirect. The selected studies examined the pathological effects of MNPs as NEDs in humans, their main exposure sources, key mechanisms of action, and their growing threat to public health.

The neuroendocrine disrupting hypothesis

The neuroendocrine disruption hypothesis was first proposed in 1991 by a group of scientists who defined the concepts of bioaccumulation, long latency between exposure and symptom presentation, and critical windows of susceptibility, including gestation and the perinatal period.¹² One of the clearest pieces of evidence supporting the neuroendocrine disruption hypothesis comes from the Estrogenic Pharmaceutical Diethylstilbestrol (DES), which was administered in clinical practice to pregnant women to prevent miscarriage.¹³ Newborns exposed to high levels of DES during gestation appeared anatomically normal at birth, but females later in life showed a higher incidence of abnormalities of the reproductive tract and an increased prevalence of vaginal and cervical cancer.¹⁴ This tragic event provided clear evidence that prenatal exposure to a drug or toxic substance can reprogram susceptibility to disease later in life, both during childhood and adulthood, linking the neuroendocrine disruption hypothesis with the Barker hypothesis of fetal programming of adult diseases.^{15,16} The DES case opened a window on the potential impact of exposure to NEDs during gestation on fetal neuroendocrinology, a research field that is still in its infancy. Several studies suggest that fetal exposure to endocrine disruptors may interfere with reproductive neuroendocrinology.¹⁷

Neuroendocrine disruptors

According to the United States Environmental Protection Agency (EPA), Endocrine-Disrupting Chemicals (EDCs) are exogenous substances or mixtures that alter the structure or function of the endocrine system and cause adverse effects. NEDs are more specifically defined as environmental pollutants that act as agonists, antagonists, or modulators of the synthesis and metabolism of neurotransmitters, ultimately producing alterations in hormonal processes that regulate development, reproduction, growth, stress responses, and other physiological functions.¹⁸ In 2018, the European Food Safety Authority (EFSA) and the European Chemicals Agency (ECHA) published guidance for the identification of endocrine disruptors, which currently represents a key reference framework for researchers investigating NEDs.¹⁹ This guidance contains the strategy to assess whether a substance meets the endocrine disruptor criteria.

Examples of well-known NEDs include the following.

Microplastics and nanoplastics

Global plastic production has increased dramatically over the past decades, exceeding 368 million tons in 2019 and permeating nearly every aspect of modern life and the environment.²⁰ The principal process utilized in plastic production is polymerization, a process that is rarely reversible to give rise to the starting oligomers.²¹ Plastic waste undergoes fragmentation, breaking down into microplastics (<5 mm) and nanoplastics (<0.1 μm).²² Nanoplastics and microplastics may be detected in food, particularly in sea food²³ as well as in personal care products²⁴ and may have a relevant impact on human health.²⁵

Phthalates

Phthalates are a family of widely used plasticizers in the Polyvinyl Chloride (PVC) industry.²⁶ PVC products discarded after use can release phthalates, contaminating groundwater and soil and entering the food chain. Children are particularly vulnerable to phthalate exposure because these compounds are present in many plastic toys. Regarding their mechanism of toxicity, phthalates can induce mitochondrial dysfunction²⁷ and induce apoptosis of neurons.²⁸

Bisphenols

Bisphenols are chemical compounds commonly used in the inner coating of aluminum cans and other polymer materials, with potential leaching into food and beverages.²⁹ They can damage the nervous and endocrine systems by mimicking estrogen pathways.³⁰ Bisphenol A has been detected in maternal breast milk and in tissues of lactating newborns even in the absence of known environmental exposure.^{31,32}

Pesticides

Multiple pesticides, including DDT, glyphosate, atrazine, and chlorpyrifos, possess neuroendocrine-disrupting properties.³³ Human exposure occurs through occupational activities and dietary intake. Pesticides may interfere with androgen and estrogen receptor activity.³⁴ The global use of agricultural pesticides has increased in recent years, contributing to widespread human exposure through multiple environmental pathways, including groundwater, surface water, soil, food, and drinking water.³⁵ Exposure to pesticides has been associated with congenital anomalies, reproductive disorders, and cancer through their endocrine-disrupting properties.³⁶

Dioxins

Dioxins are potent environmental pollutants that act as neuroendocrine disruptors, causing developmental and neurological abnormalities through long-term effects on DNA methylation.³⁷ The most toxic dioxin, TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin), can disrupt hormone signaling and interfere with human embryonic development through oxidative damage and mitochondrial dysfunction.³⁸ In addition to disrupting hormonal signaling, dioxins can impair immune function and have been associated with liver disease and cancer.³⁹

The mechanisms through which NEDs interfere with the human endocrine system and physiological processes are multiple and partly unknown. Some endocrine-disrupting chemicals have been shown to disrupt the integrity of the air–blood barrier in the lungs, allowing noxious substances and microbes to penetrate lung tissue, thereby increasing the risk of infections.⁴⁰ Organochlorine pesticides can agonize or antagonize hormone receptors, adversely affecting crosstalk between neurotransmitter systems.⁴¹ Most NEDs likely act by altering endogenous hormone concentrations or availability, or by modifying hormone receptor turnover, whereas a smaller proportion act as hormones by binding to and activating hormone receptors.⁴² Recent studies on the intracellular free concentration of endocrine-disrupting chemicals have confirmed that some NEDs can activate estrogen receptor alpha, thereby disrupting normal endocrine function.⁴³

Some NEDs impair neurotransmission, with severe consequences for neurological health. Recent studies have shown an association between exposure to NEDs and neurodegenerative diseases such as Alzheimer's and Parkinson's disease, as well as an increased risk of autism spectrum disorder.⁴⁴ Exposure to Polychlorinated Bisphenyls (PCB) has been associated with an increased risk for neurodegenerative diseases.⁴⁵ Some studies have shown that NEDs exert detrimental effects on central dopaminergic neurons, which may contribute to neurodevelopmental disorders, leading to impaired memory and cognitive function. NEDs, such as microplastics, phthalates, and bisphenol A, induce oxidative stress by increasing the production of Reactive Oxygen Species (ROS) and depleting antioxidant defenses in target cells.⁴⁶ Another relevant effect related to NEDs at cellular level, is represented by mitochondrial dysfunction. Mitochondrial dysfunction might play a crucial role in cellular energy generation, increasing the susceptibility to the insurmountable of type 2 diabetes in exposed subjects.⁴⁷ Immune dysregulation is another possible consequence of exposure to NEDs. Immune and mitochondrial dysfunction, both induced by endocrine disruptors, have been associated with an increased risk of Alzheimer's disease.⁴⁴

NEDs can also modify epigenetic markers, such as DNA methylation status, and induce histone modifications. Disruption of these processes by endocrine disruptors during the perinatal period may lead to long-term reprogramming of DNA methylation and sex steroid hormone receptor expression.⁴⁸ Exposure to some NEDs, including phthalates and bisphenol A, has been associated with abnormalities of the hypothalamic-pituitary axis, that plays a critical role in the control of the endocrine system.⁴⁹ NEDs might interfere with hormone synthesis, metabolism and action, leading to relevant endocrine irregularities. When neuroendocrine homeostasis is disrupted by NEDs, a variety of perturbations can ensue, particularly on endocrine and reproductive functions.⁵⁰

Major sources of NEDs exposure

Humans are exposed daily to numerous potentially harmful chemicals, including compounds with neuroendocrine-disrupting properties. These substances may enter the body through multiple exposure routes, including ingestion, inhalation, and dermal absorption. Although exposure levels are often low, chronic exposure over long periods may result in significant adverse health effects later in life. The main sources of NED exposure are summarized below.

Water contamination

As the global consumption of pharmaceuticals increases, including in low-resource settings, surface waters are becoming increasingly contaminated with a wide range of pharmaceutical compounds, including Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), antibiotics, synthetic estrogens, beta-blockers, and Selective Serotonin Reuptake Inhibitors (SSRIs).⁵¹ Numerous pharmaceutical compounds are increasingly detected in aquatic environments, including the selective serotonin reuptake inhibitor fluoxetine (Prozac), which has been implicated in neuroendocrine disruption.⁵²

Food contamination

In recent years, MNPs have increasingly entered the food supply, raising concerns about potential risks to human health.⁵³ Furthermore, phthalates have been reported in food packaging and other food-contact materials.⁵⁴ Bisphenol A, widely used in the production of epoxy resins and polymer-based materials, has been detected in food.⁵⁵

Cosmetics

The presence of nanoplastics in cosmetic products has been reported in several studies. Their ability to cross the skin barrier and enter the bloodstream has raised concerns and prompted calls for stricter regulation or potential bans.⁵⁶

Electronic waste

In the context of neuroendocrine disruptor pollution, electronic waste (e-waste) is emerging as an important source of microplastic and heavy metal contamination. This issue is particularly relevant in developing countries, where discarded electronic devices are often processed in informal dumping sites, leading to mechanical fragmentation into microplastics that contaminate soil and water.⁵⁷

Agricultural pesticides

In recent years, microplastics and nanoplastics in agricultural systems have raised concerns regarding plant health and potential risks to human health.⁵⁸ The accumulation of microplastics in soil is often associated with the presence of heavy metals and pesticides, with potential effects on plant physiology and implications for food quality and safety.

Conflicting research findings regarding human toxicity of neuroendocrine disruptors

Conflicting results in the literature regarding human toxicity associated with exposure to NEDs mainly arise from the complexity of exposure scenarios, challenges in assessing low-dose effects,

and variability in experimental methods across studies.⁵⁰ Discrepancies among experimental studies often stem from the use of different study protocols, animal models or cell lines.⁵⁹

Studies in pregnant animals investigating the effects of NEDs on the fetal brain at different developmental stages have often produced conflicting results, likely due to changes in brain sensitivity during specific embryological stages. The use of different animal models, such as mice, rats, and zebrafish, may also contribute to inconsistent findings, given species-specific differences in metabolic rates and sensitivity to chemicals. It should also be considered that translating findings from animal studies to humans remains a persistent challenge in literature.

A key issue in evaluating the effects of NEDs is the so-called “cocktail effect”.^{60,61} While most experimental data focus on exposure to a single endocrine disruptor, real-world human exposure rarely involves a single factor but rather a “cocktail” of substances, including nanoplastics, microplastics, phthalates, bisphenols, pesticides, and pharmaceuticals.⁶² The combined effects of multiple NEDs can be synergistic or antagonistic, contributing to conflicting findings regarding their toxicity.

Taken together, these challenges highlight the lack of a comprehensive body of literature on global research efforts addressing human toxicity due to exposure to NEDs, with low- and middle-income countries underrepresented in both research and epidemiological data on endocrine disruptors.⁶³ In short, there are limitations of current knowledge regarding the influence of NEDs on human health, that induced some authors to define it “the invisible influence”.⁶⁴

High-risk subjects and vulnerability in low-resource setting populations

Pregnant women and fetuses

Microplastic pollution represents a growing concern for human health because of its potential to impair fetal development during gestation. Microplastics of varying sizes have been detected in the placenta and fetal tissues, where they may influence the fetal intestinal microbiome and have been associated with reduced birth weight and impaired fetal growth.⁶⁵ Furthermore, exposure to nanoplastics during pregnancy has been shown to alter microglial activity and neuronal differentiation in the fetal brain, affecting neurotransmitter levels and synaptic integrity.⁶⁶ Understanding how microplastics and nanoplastics affect pregnancy and maternal–fetal health remains a major challenge for the scientific community.⁶⁷ Microplastics and nanoplastics have been detected in the neonatal brain after crossing the blood–brain barrier, where they may induce oxidative stress and neuroinflammation and have been associated with behavioral alterations in newborns.⁶⁸ According to several authors, the perinatal period represents a particularly vulnerable window of exposure, during which multipotent stem/progenitor cells present in breast milk may act as carriers of MNPs and other NEDs to the developing brain of the newborn.

Children

Infancy and childhood represent sensitive windows of vulnerability to environmental exposure to MNPs, largely due to the immaturity of physiological defence mechanisms.⁶⁹ Although the health effects of MNPs remain poorly understood, the detection of these particles in blood and myocardial tissue raises concerns about early-life exposure.⁷⁰

Adolescents

Exposure to MNPs during adolescence has been reported to induce cognitive impairments in experimental animals, including inhibition of neurogenesis and cell damage in the hippocampus.⁷¹

Occupational workers

Workers in textile industries, plastic manufacturing, 3D printing, and waste management are exposed to higher concentrations of inhaled MNPs compared with the general population.⁷² In occupational settings, the primary route of exposure is the inhalation of airborne particles.⁷³ The degradation of carpets and other synthetic fiber products can release airborne fibers rich in MNPs.⁷⁴

Challenges in health status protection against NEDs in low-resource settings

Waste mismanagement, one of the major drivers of environmental contamination by neuroendocrine disruptors, including MNPs, disproportionately affects low- and middle-income countries, particularly in Africa.⁷⁵ In particular, Sub-Saharan Africa faces increasing levels of plastic production and imports which, combined with inadequate waste management, contribute to widespread plastic pollution with significant environmental and public health impacts.⁷⁶ Plastic pollution represents a critical issue in many African countries, driven by limited waste management and recycling capacity. Approximately 17 million tons of plastic waste are generated annually, with around 80% ending up in landfills or the environment and less than 9% being recycled.^{77,78} With plastic production projected to double over the next 20 years, African countries are expected to face severe impacts from plastic pollution in the absence of immediate action, posing significant risks to marine life and human health.⁷⁹ Despite the African Union’s goal to increase plastic waste recycling, the continent faces significant barriers to achieving this target in low-resource settings due to economic, infrastructural, and social challenges.⁸⁰ Pyrolysis technology has been proposed as a viable solution to plastic waste management, as it can convert plastic into byproducts such as oil, char and syngas.⁸¹ To address plastic pollution in developing countries, the implementation of mitigation strategies is essential.⁸² In rural communities affected by plastic pollution, plastic waste management may represent an opportunity by fostering circular economy initiatives and supporting low-income populations.⁸³ The implementation of plastic bag bans in Rwanda, Kenya, and Uganda has enabled these countries to adopt circular economy and sustainable policies, with encouraging environmental outcomes.⁸⁴ In Nigeria, the introduction of a plastic ban has contributed to reducing marine plastic pollution, highlighting a pathway for environmental protection policies targeting NEDs and micro- and nanoplastic pollution.⁸⁵

In low-income Asian countries, plastic pollution is a widespread and major problem, mainly related to limited waste management infrastructure and, as in many African countries, to the large-scale import of plastic waste from developed countries.⁸⁶ Countries such as Malaysia, Vietnam, and Cambodia are affected by “waste colonialism”, characterized by the import of plastic waste from high-income countries, often in the absence or scarcity of local infrastructure to manage it, resulting in environmental damage. Improper plastic waste management poses health risks to local populations, particularly to communities that rely on fishing. Low-income countries in South and Southeast Asia have witnessed

an unprecedented increase in aquatic and terrestrial plastic and MNPs pollution in soil, water, and air.⁸⁷ Regional policies to address plastic and microplastic pollution have been proposed in recent years in several South Asian countries, including India, Bangladesh, the Maldives, Sri Lanka, and Pakistan.⁸⁸

Mismanagement of plastic waste often results in marine plastic pollution, environmental degradation, and health risks for local communities.⁸⁹ High poverty rates drive the consumption of low-cost food packaged in single-use plastic sachets, which are difficult to recycle.

Potential mitigation strategies aimed to halt NEDs epidemics

Remediation technologies, together with institutional and legislative measures for improved waste management of MNPs, represent key strategies to reduce pollution from NEDs and human exposure, particularly in low- and middle-income countries.⁹⁰ Moreover, addressing plastic pollution requires a coordinated set of strategies aimed at monitoring plastic production and improving waste management, supported by appropriate regulatory measures.⁹¹ In summary, a comprehensive policy framework is needed to better address the environmental impacts affecting populations in low-resource countries and the human health risks associated with exposure to plastics and other NEDs.⁹²

In low-income countries characterized by high levels of MNP water pollution, novel strategies should be implemented to prevent population overexposure, given that prolonged MNP release poses a significant threat to ecosystems and their inhabitants.⁹³ The removal of micro-nanoplastics originated from diverse sources requires innovative technologies capable of effectively eliminating them from the environment.⁹⁴ Various remediation techniques have been proposed to address MNP pollution, including physical, chemical, and microbial bioremediation approaches, as well as adsorption, offering promising avenues to tackle this global issue. Among these methods, biotechnological approaches stand out as effective and sustainable solutions for managing NEDs and other toxic compounds. Recently, novel membrane separation processes have attracted considerable attention due to their high efficiency in removing MNPs. Through these methods, dissolved organic matter, extracellular polymers, and suspended particles, including nanoplastics and microplastics, can be retained on the membrane surface. On this basis, the removal of MNPs from drinking water in low-income countries affected by river pollution appears to be an achievable goal in the coming years. In the field of MNP removal from wastewater, micro/nanorobots have been proposed as a promising solution to improve water monitoring and efficiently remove MNPs. These systems can capture MNPs through electrostatic adsorption and electrophoretic interactions, followed by separation under the action of an external rotating magnetic field. Although micro/nanorobots appear to be a promising technology for the removal of MNPs from water, their applications still require further investigation. Magnetic nanomaterials, such as iron oxide nanoparticles, as well as magnetic nanocomposites, have recently been proposed as novel remediation strategies for MNP pollution in terrestrial and aquatic environments.

Conclusions

Research on NEDs has increasingly been recognized as an

important issue for both human health and environmental protection.² This field of research is still evolving, as many questions remain unanswered regarding the numerous substances capable of disrupting the neuroendocrine system and the mechanisms of action of many neuroendocrine disruptors, which remain only partially understood.⁹⁵ In this complex scenario, low- and middle-income countries remain underrepresented in scientific research, despite the fact that populations living in low-resource settings are among the most vulnerable to the effects of NEDs due to the high levels of environmental contamination often present in these regions. There is a growing need for risk assessment of exposure to endocrine disruptors and for initiatives aimed at reducing exposure. Additional precaution is required to address this global health challenge.

In this review, we have summarized the most relevant findings from the literature on the high levels of plastic, particularly MNP, pollution in the environment, with low-income countries representing the most exposed and vulnerable regions worldwide. In this context, a key finding is the limited awareness of the general population on this issue, especially in low-income settings, where exposure to MNPs and NEDs is highest.

We have also highlighted several methods developed to address MNP pollution in water, which may support the future development of government policies aimed at improving drinking water quality by reducing contamination from MNPs and other neuroendocrine disruptors. However, some of these technologies, such as nanorobots, remain costly and are not readily accessible in low-resource countries.

Future research should be supported by governments to promote the development of affordable and effective technologies for mitigating water contamination by MNPs, neuroendocrine disruptors, and other toxicants. The EU-funded ENDOMIX project represents an important model for low-resource countries seeking to better understand how everyday exposure to chemicals with neuroendocrine-disrupting properties affects human health. ENDOMIX, funded by the European Union's Horizon Europe research and innovation program (grant agreement No. 101136566), aims to address several relevant questions regarding the impact of exposure to NEDs on human health; i) how do NEDs interfere with or modify neuroendocrine processes in the human body? ii) What are the potential consequences of NED exposure for human health? iii) Which diseases may be caused or exacerbated by NED exposure, particularly asthma, allergies, reproductive disorders, and metabolic syndrome? iv) How do NEDs act as mixtures in the human body, with particular attention to the "cocktail effect"? v) What are the critical windows of susceptibility during which the body is particularly sensitive to exposure to NEDs?

The ENDOMIX project could represent a valuable model for low-resource countries seeking to develop initiatives aimed at protecting their populations from exposure to NEDs and implementing preventive measures to reduce associated health risks. Preventive programs should provide practical recommendations to help individuals limit everyday exposure to chemicals with hormonal and neuroendocrine effects. Addressing this important public health challenge in low- and middle-income countries will require coordinated efforts from authorities, the scientific community, industry, and the active participation of the population.⁹⁶

Finally, Artificial Intelligence (AI) may represent a novel tool for the detection of microplastics. A deep-learning system has recently been developed that is capable of rapidly detecting microplastics in consumer products at low cost, with an accuracy of approximately 98%.⁹⁷ This fast and accurate AI-driven method

could facilitate cost-effective detection of microplastics and, particularly in low-resource settings, enable the monitoring of microplastic content in consumer products, providing a basis for strategies aimed at reducing microplastic pollution.

References

1. Ali N, Katsouli J, Marczylo EL, Gant TW, Wright S, Bernardino De La Serna J. The potential impacts of micro-and-nano plastics on various organ systems in humans [Internet]. 2023. Available from: <http://creativecommons.org/licenses/by/4.0/>
2. Klingelhöfer D, Braun M, Dröge J, et al. Global research on endocrine disruptors as emerging hazards for human health and the environment. *Front Endocrinol (Lausanne)* 2025;16:1561711.
3. Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, et al. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocr Rev* 2009;30:293-342.
4. Kahn LG, Philippat C, Nakayama SF, et al. Endocrine-disrupting chemicals: implications for human health. *Lancet Diabetes Endocrinol* 2020;8:703-18.
5. Dube E, Okuthe GE. Environmental exposure to endocrine disruptors in developing countries. *Int J Environ Res Public Health* 2023;20:6667.
6. Ullah S, Ahmad S, Guo X, Ullah S, Ullah S, Nabi G, et al. A review of the endocrine disrupting effects of micro and nano plastic and their associated chemicals in mammals. *Frontiers in Endocrinology*. *Front Endocrinol (Lausanne)* 2023;13:1084236.
7. Tyc HJ, Kłodnicka K, Teresińska B, et al. Micro- and nanoplastics as disruptors of the endocrine system – a review of the threats and consequences associated with plastic exposure. *Int J Mol Sci* 2025;26:6156.
8. Bossio S, Ruffolo SA, Lofaro D, et al. Endocrine toxicity of micro- and nanoplastics, and advances in detection techniques for human tissues: a comprehensive review. *Endocrines*. 2025;6:23
9. Yang S, Li M, Kong RYC, et al. Reproductive toxicity of micro- and nanoplastics. *Environ Int* 2023;177:108002.
10. Talaie A, Alaei S, Hosseini E, et al. Toxicological effects of micro/nano-plastics on human reproductive health: A review. *Toxicol Lett* 2025;412:1-20.
11. Zhu X, Wang C, Duan X, et al. Micro- and nanoplastics: A new cardiovascular risk factor? *Environ Int* 2023;171:107662.
12. Gore AC, Patisaul HB. Neuroendocrine disruption: historical roots, current progress, questions for the future. *Front Neuroendocrinol* 2010;31:395-399.
13. McLachlan JA, Dixon RL. Toxicologic comparison of experimental and clinical exposure to diethylstilbestrol during gestation. *Adv Sex Steroid Horm Res* 1977;3:309-36.
14. Herbst AL, Ulfelder H, Poskanzer DC. Adenocarcinoma of the vagina: association of maternal stilbestrol therapy with tumor appearance in young women. *N Engl J Med* 1971;284:878-81.
15. Barker DJP. Maternal nutrition, fetal nutrition, and disease in later life. *Nutrition*. 1997;13:807-13.
16. Faa G, Fanos V, Manchia M, et al. The fascinating theory of fetal programming of adult diseases: a review of the fundamentals of the Barker hypothesis. *J Public Health Res* 2024;13:1-10.
17. Gore AC. Developmental programming and endocrine disruptor effects on reproductive neuroendocrinology. *Front Neuroendocrinol* 2008;29:358-374.
18. Wayne A, Trudeau VL. Neuroendocrine disruption: more than hormones are upset. *J Toxicol Environ Health B Crit Rev* 2011;14:270-291.
19. Andersson N, Arena M, Auteri D, et al. Guidance for the identification of endocrine disruptors. *EFSA J* 2018;16:e05311.
20. Wagner M, Scherer C, Alvarez-Muñoz D, et al. Microplastics in freshwater ecosystems: what we know and what we need to know. *Nat Nanotechnol* 2019;14:300-1.
21. Luo H, Tyrrell H, Bai J, et al. Fundamental, technical and environmental overviews of plastic chemical recycling. *Green Chem* 2024;26:11444-67.
22. Gigault J, Halle AT, Baudrimont M, et al. Current opinion: what is a nanoplastic? *Environ Pollut* 2018;235:1030-1034.
23. EFSA Panel on Contaminants in the Food Chain. Presence of microplastics and nanoplastics in food. *EFSA J* 2016;14:4501.
24. Hernandez LM, Xu EG, Larsson HCE, et al. Plastic teabags release billions of microparticles. *Environ Sci Technol Lett* 2017;4:280-5.
25. Yee MS, Hii LW, Looi CK, et al. Impact of microplastics and nanoplastics on human health. *Nanomaterials (Basel)* 2021;11:496.
26. Amara I, Timoumi R, Graiet I, et al. Phthalates in the environment and human health. *Environ Toxicol* 2019;34:1034-42.
27. Ashari S, Karami M, Shokrzadeh M, et al. Mitochondrial dysfunction induced by phthalates. *Toxicol Mech Methods* 2020;30:427-37.
28. Aung KH, Win-Shwe TT, Kanaya M, et al. Phthalate-induced neuronal apoptosis. *J Toxicol Sci*. 2014;39:217-29.
29. Almeida S, Raposo A, Almeida-González M, Carrascosa C. Bisphenol exposure through food packaging. *Compr Rev Food Sci Food Saf* 2018;17:1503-17.
30. Kaulgud RS, Belur S, Anagharani AM, Veeresh S, Shettar AK. Bisphenols and endocrine disruption. *Discover Toxicol* 2025;2:24.
31. Mendonca K, Hauser R, Calafat AM, et al. Bisphenol A exposure in lactating women and infants. *Int Arch Occup Environ Health* 2012;87:13-20.
32. Ahmadpourmir H, Moradzei M, Velayati M, et al. Bisphenol contamination in food products. *Food Res Int* 2025;211:116389.
33. Mnif W, Hassine AI, Bouaziz A, et al. Effect of endocrine disruptor pesticides: a review. *Int J Environ Res Public Health* 2011;17:2265-2303.
34. Lemaire G, Mnif W, Mauvais P, et al. Activation of alpha- and beta-estrogen receptors by persistent pesticides in reporter cell lines. *Life Sci* 2006;79:1160-9.
35. Kolpin DW, Furlong ET, Meyer MT, et al. Pharmaceuticals, hormones and contaminants in U.S. streams. *Sci Total Environ* 2000;248:115-122.
36. Kumar V, Sharma N, Sharma P, et al. Endocrine disrupting pesticides and human health. *Toxicol Appl Pharmacol* 2023;474:116623.
37. Sacco D, Brambilla P, Calzari L, et al. Dioxin, an endocrine disruptor, induces long term effects on DNA methylation in men after in-utero exposure. *Minerva Endocrinol (Torino)* 2026;51:150-60.
38. Chen SC, Liao TL, Wei YH, et al. TCDD effects on human embryonic development. *Mol Hum Reprod* 2010;16:361-372.
39. Kafouris D. Exposure Assessment in Dioxins & Dioxin-like PCBs. *Food Risk Assess Europe* 2025;3:0081E.

40. Molinari F, Franco GA, Tranchida N, et al. Molecular mechanism of action of endocrine-disrupting chemicals on the respiratory system. *Int J Molecular Sci* 2024;25:12540.
41. León-Olea M, Martyniuk CJ, Orlando EF, et al. Current concepts in neuroendocrine disruption. *Gen Comp Endocrinol* 2014;203:158-73.
42. Combarous Y, Diep Nguyen TM. Comparative overview of the mechanisms of action of hormones and endocrine disruptor compounds. *Toxics* 2019;7:5.
43. Munic Kos V, Arvidsson S, Islam B, et al. The intracellular free concentration of endocrine disrupting chemicals enables translation between cell-free and cell-based estrogenic activity assays. *Environ Toxicol Pharmacol* 2025;117:104750.
44. Karatoprak K, Cander S. Effects of endocrine disruptors on the neurological system. *Turkish Journal of Medical Sciences. TUBITAK*; 2025. p. 1657-63.
45. Wang C, Xu J, Pan K, Xu Y, Yu J. Relationship between endocrine disruptors and neurodegenerative diseases: Systematic review and meta-analysis. *iScience* 2025;28:112779.
46. Kovacs K, Bodis J, Vass RA. Microplastics, endocrine disruptors, and oxidative stress: mechanisms and health implications. *Int J Mol Sci* 2025;27:399.
47. He K, Chen R, Xu S, et al. Environmental endocrine disruptor-induced mitochondrial dysfunction: a potential mechanism underlying diabetes and its complications. *Front Endocrinol (Lausanne)* 2024;15:1422752.
48. Walker DM, Gore AC. Epigenetic impacts of endocrine disruptors in the brain. *Front Neuroendocrinol* 2017;44:1-26.
49. Graceli JB, Dettogni RS, Merlo E, et al. The impact of endocrine-disrupting chemical exposure in the mammalian hypothalamic-pituitary axis. *Mol Cell Endocrinol* 2020;518:110997.
50. Gore AC. Neuroendocrine targets of endocrine disruptors. *Hormones (Athens)* 2010;9:16-27.
51. Corcoran J, Winter MJ, Tyler CR. Pharmaceuticals in the aquatic environment: a critical review. *Crit Rev Toxicol* 2010;40:287-304.
52. Mennigen JA, Stroud P, Zamora JM, et al. Pharmaceuticals as neuroendocrine disruptors: lessons from fish on Prozac. *J Toxicol Environ Health B* 2011;14:387-412.
53. Vitali C, Peters RJB, Janssen HG, Nielen MWF. Microplastics and nanoplastics in food, water, and beverages; part I. occurrence. *Trends Analyt Chem* 2023;159:116670.
54. Schecter A, Lorber M, Guo Y, et al. Phthalates in food packaging. *Environ Health Perspect* 2013;121:473-9.
55. Manzoor MF, Tariq T, Fatima B, et al. Bisphenol A contamination in food systems. *Front Nutr* 2022;9:104827.
56. Joksimovic N, Selakovic D, Jovicic N, et al. Nanoplastics in cosmetics and potential human exposure. *J Nanomater* 2022:6707819.
57. Shaaban M, Wang X.L; Song P, et al. Electronic waste as a source of microplastic pollution. *Chemosphere* 2024;346:100891.
58. Wolff Leal T, Tochetto G, Lima SVdM, et al. Nanoplastics and microplastics in agricultural systems: effects on plants and implications for human consumption. *Microplastics* 2025;4:16.
59. Alofe O, Kisanga E, Inayat-Hussain SH, et al. Determining the endocrine disruption potential of industrial chemicals using an integrative approach: Public databases, in vitro exposure, and modeling receptor interactions. *Environ Int* 2019;131:104969.
60. Kortenkamp A. Ten years of mixing cocktails: A review of combination effects of endocrine-disrupting chemicals. *Environ Health Perspect* 2007;115:98-105.
61. Zhao S, Dong J, Luo Z. The associations between exposure to mixed environmental endocrine disruptors and sex steroid hormones in men: a comparison of different statistical models. *Sci Rep* 2024;14:26375.
62. Ye T, Yang R, He S, et al. Synergistic endocrine disruption and cellular toxicity of polyethylene microplastics and bisphenol A in MLTC-1 cells and zebrafish. *Sci Rep* 2025;15:10752.
63. Pan S, Li Z, Rubbo B, et al. Applications of mixture methods in epidemiological studies investigating the health impact of persistent organic pollutants exposures: a scoping review. *J Expo Sci Environ Epidemiol* 2025;35:522-534.
64. Damiano A, Caioni G, D'Addario C, et al. The invisible influence: can endocrine disruptors reshape behaviors across generations? *Stresses* 2025;5:46.
65. Sharma RK, Kumari U, Kumar S. Impact of microplastics on pregnancy and fetal development: a systematic review. *Cureus* 2024;16:e60712.
66. Tian L, Zhang Y, Chen J, et al. Nanoplastics alter neuronal differentiation in the fetal brain. *J Hazard Mater* 2024;474:134800.
67. Panneerselvam D, Murugesan A, Raveendran SK, et al. Microplastics exposure and pregnancy outcomes. *Eur J Obstet Gynecol Reprod Biol* 2025;304:P53-P62.
68. Ragusa A, Fanos V. Microplastics and nanoplastics in the brain. *JPNIM* 2025;14:e140206.
69. Xia, W. Unraveling the early-life impacts of environmental exposures: from fetal growth to child development. *Toxics* 2025;13:849.
70. Lv L, Lang X, Sun Y, et al. Detection of nanoplastics in blood and myocardial tissue. *Environ Technol Innov* 2025;40:104371.
71. Comisi FF, Comisi AM, Esposito E, Fanos V. Exposure to microplastics in biological matrices and neurodevelopmental outcomes in children: a systematic review. *Nanomaterials* 2026;16:618.
72. Murashov V, Geraci CL, Schulte PA, Howard J. Nano- and microplastics in the workplace. *J Occup Environ Hyg* 2021;18:489-94.
73. Stefaniak AB, Johnson AR, du Preez S, et al. Exposure to airborne particles in occupational environments. *Saf Health Work* 2019;10:229-36.
74. Dris R, Gasperi J, Saad M, et al. Synthetic fibers in atmospheric fallout: A source of microplastics in the environment? *Mar Pollut Bull* 2016;104:290-3.
75. Ferronato N, Torretta V. Waste mismanagement in developing countries: a review of global issues. *Int J Environ Res Public Health* 2019;16:1060.
76. Dube E, Okuthe GE. Plastic and micro/nanoplastic pollution in Sub-Saharan Africa: challenges, impacts, and solutions. *World* 2024;5:325-45.
77. Adeniran AA, Ayesu-Koranteng E, Shakantu W. A review of the literature on the environmental and health impact of plastic waste pollutants in Sub-Saharan Africa. *Pollutants* 2022;2:531-45.
78. Shomuyiwa DO, Onukansi FO, Ivanova M, Lucero-Prisno DE 3rd. The Plastic treaty: What is in it for Africa? *Public Health Chall* 2023;2:e83.
79. Babayemi JO, Nnorom IC, Osibanjo O, Weber R. Ensuring sustainability in plastics use in Africa: consumption, waste

- generation, and projections. *Environ Sci Eur* 2019;31:60.
80. Ayeleru OO, Dlova S, Akinribide OJ, et al. Challenges of plastic waste generation and management in sub-Saharan Africa: A review. *Waste Manag* 2020;110:24-42.
 81. Dennison MS, Paramasivam SK, Wanazusi T, et al. Addressing plastic waste challenges in Africa: the potential of pyrolysis for waste-to-energy conversion. *Clean Technol* 2025;7:20.
 82. Hira A, Pacini H, Attafuah-Wadee K, et al. Plastic waste mitigation strategies: a review of lessons from developing countries. *J Dev Soc* 2022;38.
 83. Mihai FC, Gündogdu S, Markley LA, Olivelli A, Khan FR, Gwinnett C, et al. Plastic pollution, waste management issues, and circular economy opportunities in rural communities. *Sustainability* 2022;14:20.
 84. Behuria P. Ban the (plastic) bag? Explaining variation in the implementation of plastic bag bans in Rwanda, Kenya and Uganda. *Environment and Planning C: Politics and Space*. 2021;39:1791-808.
 85. Nwafor N, Walker TR. Plastic Bags Prohibition Bill: A developing story of crass legalism aiming to reduce plastic marine pollution in Nigeria. *Mar Policy* 2020;120:104160.
 86. Anthony J, Varalakshmi S, Kumar Sekar A, et al. Microplastics pollution in Indian marine environment: sources, effects and solutions. *Front Marine Sci* 2024;11:1512802.
 87. Pandey A, Asif M. Assessment of energy and environmental sustainability in South Asia in the perspective of the Sustainable Development Goals. *Renewable Sustainable Energy Rev* 2022;165:112492.
 88. Rifa T, Hossain MB. Micro plastic pollution in South Asia: the impact of plastic pollution over the unsustainable development goals. *Lex Publica* 2023;9(2).
 89. Khuyen VTK, Le DV, Anh LH, Fischer AR, Dornack C. Investigation of microplastic contamination in vietnamese sea salts based on raman and fourier-transform infrared spectroscopies. *Environment Asia* 2021;14:11.
 90. Arif Y, Mir AR, Zieliński P, et al. Microplastics and nanoplastics: Source, behavior, remediation, and multi-level environmental impact. *J Environ Manage* 2024;356:120618.
 91. Kochanek A, Graż K, Potok H, et al. Micro- and nanoplastics in the environment: current state of research, sources of origin, health risks, and regulations – a comprehensive review. *Toxics* 2025;13:564.
 92. Amobonye A, Bhagwat P, Raveendran S, et al. Microplastic pollution and environmental health risks. *Front Microbiol* 2021;12:768297.
 93. Adegoke KA, Adu FA, Oyebamiji AK, et al. Microplastics toxicity, detection, and removal from water/wastewater. *Mar Pollut Bull* 2023;187:114546.
 94. Majeed F, Razzaq A, Rehmat S, et al. Enhanced dye sequestration with natural polysaccharides-based hydrogels: A review. *Carbohydr Polym* 2024;330:121820.
 95. Schug TT, Johnson AF. Endocrine disruptors: past lessons and future directions. *Mol Endocrinol* 2016;30:833-847.
 96. Osuna-Laveaga DR, Ojeda-Castillo V, Flores-Payán V, Gutiérrez-Becerra A and Moreno-Medrano ED (2023) Micro- and nanoplastics current status: legislation, gaps, limitations and socio-economic prospects for future. *Front. Environ. Sci.* 11:1241939. doi: 10.3389/fenvs.2023.1241939
 97. Arju ZBZ, Hridi NA. Deep-learning enabled rapid low-cost detection of microplastics in consumer products. *RSC Adv* 2025;15:10473-83.

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