Available online www.worldscientificnews.com

World Scientific News

An International Scientific Journal

WSN 216 (2026) 150-190 EISSN 2392-2192

Environmental Chemistry of Emerging Contaminants and Their Anatomic Pathology Implications: From Molecular Perturbation to Tissue Lesions and Organ Dysfunction

Kanayo Samuel Okonji[1,2*] and Oluwagbenga Tosin Alade[3]

[1]Department of Chemistry, Federal University Oye-Ekiti, Ekiti State, Nigeria.
[2]Department of Health Sciences, University of the People, Pasadena, California, USA.
[3]Department of Anatomic Pathology, Ekiti State Teaching Hospital, Ado-Ekiti, Ekiti State, Nigeria.

Corresponding Author Email: kanayosamuelokonji63@gmail.com

https://doi.org/10.65770/ENFA2362

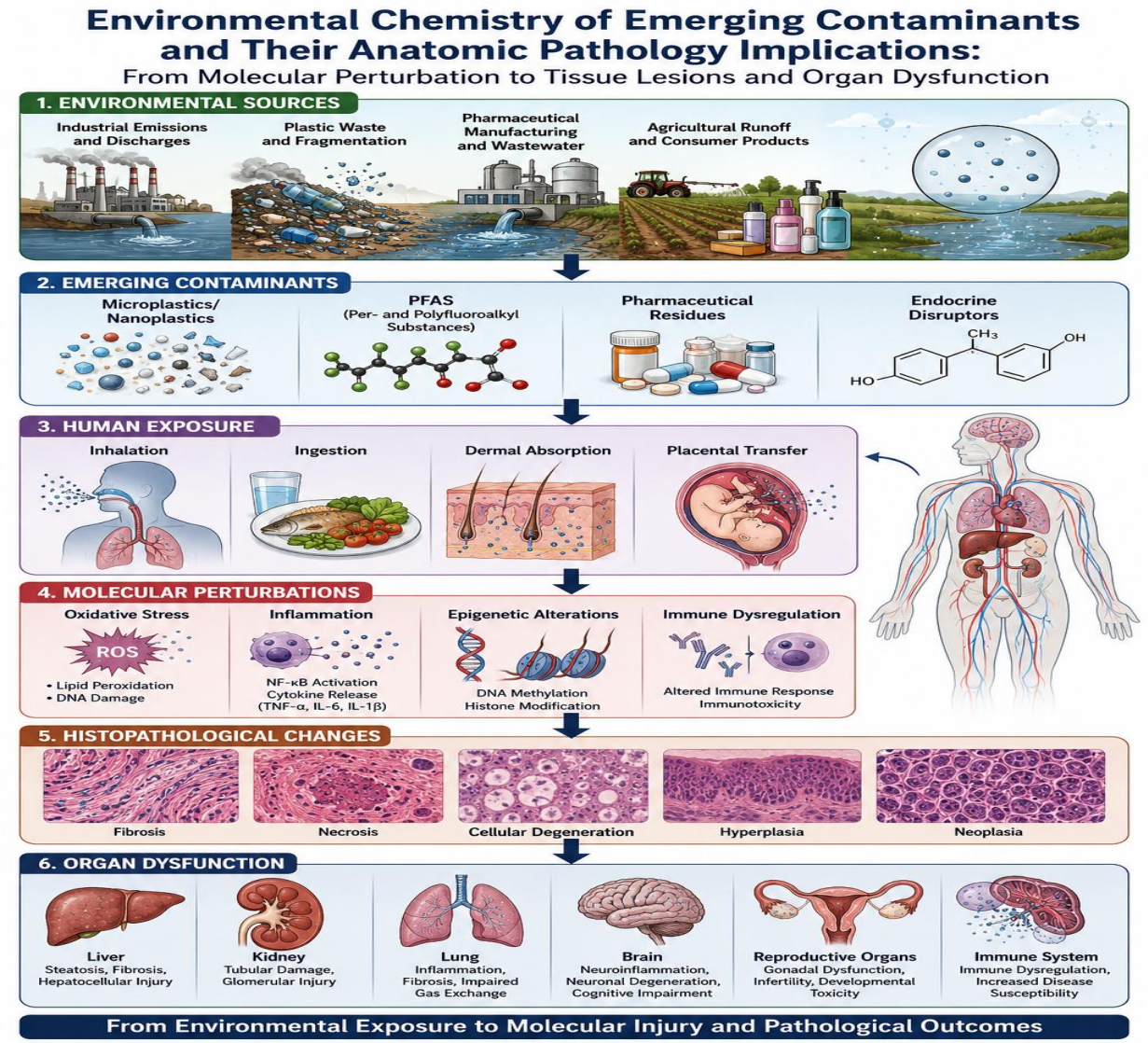
ABSTRACT

Environmental contamination has evolved beyond traditional pollutants to include a growing class of emerging contaminants such as microplastics, nanoplastics, per- and polyfluoroalkyl substances (PFAS), pharmaceutical residues, and endocrine-disrupting chemicals. These contaminants are increasingly detected in air, water, food systems, wildlife, and human tissues. While environmental chemistry has extensively characterized their occurrence, persistence, transport, and transformation, their pathological consequences remain fragmented across disciplines. This review integrates environmental chemistry with anatomic pathology by examining how emerging contaminants induce cellular and tissue-level lesions that culminate in organ dysfunction. Particular emphasis is placed on contaminant fate, bioaccumulation, oxidative stress induction, inflammatory signaling, endocrine disruption, immune dysregulation, and epigenetic modifications. Histopathological manifestations, including fibrosis, necrosis, cellular degeneration, chronic inflammation, hyperplasia, and neoplastic transformation, are discussed across major organ systems. Current evidence from human biomonitoring studies and experimental animal investigations is critically evaluated. The review highlights the need for pathology-informed environmental risk assessment frameworks and proposes future directions integrating toxicopathology, exposomics, and environmental surveillance.

Keywords: Emerging contaminants, Microplastics, PFAS, Environmental chemistry, Histopathology, Organ toxicity, Anatomic pathology.

(Received 18 April 2026; Accepted 19 May 2026; Date of Publication 30 June 2026)

GRAPHICAL ABSTRACT



1. INTRODUCTION

1.1. Emerging Contaminants as a Global Environmental Challenge

Over the past few decades, environmental pollution has evolved from concerns dominated by conventional contaminants such as heavy metals, petroleum hydrocarbons, and persistent organic pollutants to a broader and more complex spectrum of chemicals collectively referred to as emerging contaminants (ECs)[1]. Emerging contaminants encompass a diverse group of anthropogenic substances that are increasingly detected in environmental matrices but are not routinely monitored or adequately regulated. These include microplastics, nanoplastics, pharmaceutical residues, personal care products, endocrine-disrupting chemicals (EDCs), per- and polyfluoroalkyl substances (PFAS), engineered nanomaterials, and novel industrial compounds.

The widespread occurrence of emerging contaminants has become a significant environmental and public health concern due to their persistence, mobility, bioaccumulative potential, and biological activity even at low concentrations [2]. Unlike many traditional pollutants, numerous ECs are continuously introduced into ecosystems through wastewater discharges, industrial activities, agricultural runoff, landfill leachates, atmospheric deposition, and domestic consumption patterns. Their ubiquitous presence has been documented in surface waters, groundwater, marine ecosystems, soils, sediments, food products, wildlife tissues, and increasingly, human biological samples, including blood, urine, placental tissues, breast milk, and internal organs.

Among these contaminants, microplastics and nanoplastics have attracted considerable scientific attention because of their capacity to adsorb toxic chemicals, penetrate biological barriers, and accumulate within tissues. Similarly, PFAS, often referred to as "forever chemicals," exhibit exceptional environmental persistence owing to the strength of their carbon-fluorine bonds and have been associated with adverse health outcomes ranging from immune dysfunction to carcinogenesis. Pharmaceutical residues and endocrine disruptors further complicate environmental exposure scenarios by interfering with physiological and hormonal pathways in humans and wildlife [3].

The growing detection of these contaminants in human tissues raises important questions regarding their biological fate and pathological significance. While environmental monitoring studies have extensively characterized their occurrence and distribution, comparatively less attention has been directed toward understanding the structural and histological consequences of chronic exposure. Consequently, there is an increasing need for interdisciplinary frameworks capable of linking environmental contamination to observable pathological outcomes.

1.2. Evolution of Environmental Chemistry Research

Environmental chemistry has traditionally focused on identifying pollutant sources, environmental transport mechanisms, transformation processes, and ecological impacts. Early investigations primarily addressed classical contaminants such as lead, mercury, cadmium, arsenic, pesticides, and industrial solvents, emphasizing their environmental persistence and toxicological consequences. Over time, advances in analytical instrumentation, including high-resolution mass spectrometry, chromatography, and spectroscopic techniques, have substantially expanded the ability to detect contaminants at trace and ultra-trace concentrations [4].

The field has consequently transitioned from studying individual pollutants to investigating complex contaminant mixtures, transformation products, and exposure networks within interconnected environmental systems. This shift has been accompanied by the emergence of concepts such as the exposome, which seeks to characterize the cumulative environmental exposures experienced by individuals throughout their lifetime. Environmental chemistry now encompasses not only contaminant occurrence and fate but also molecular interactions, bioavailability, bioaccumulation, and mechanisms of toxicity [5].

Despite these advances, much of environmental chemistry remains focused on environmental compartments rather than biological endpoints. Measurements of contaminant concentrations in air, water, soil, and food provide essential information regarding exposure potential but offer limited insight into the structural tissue alterations that ultimately determine disease outcomes [6]. Consequently, there is increasing recognition that environmental chemistry must be integrated with biomedical disciplines capable of elucidating the biological consequences of exposure.

Recent developments in toxicology, molecular biology, omics technologies, and computational modeling have facilitated a more mechanistic understanding of contaminant-induced disease processes. However, the translation of these molecular insights into tissue-level pathology remains insufficiently explored. Bridging this gap represents a critical opportunity for advancing environmental health sciences and improving risk assessment frameworks.

1.3. Why Pathology Matters

Pathology serves as the cornerstone of disease characterization by providing direct evidence of structural and functional alterations occurring within tissues and organs. Among its branches, anatomic pathology focuses on the macroscopic, microscopic, and molecular examination of tissues to identify disease-associated lesions, characterize mechanisms of injury, and establish diagnostic criteria [7]. Histopathological evaluation remains one of the most reliable approaches for detecting tissue responses to toxic insults and environmental stressors.

Environmental contaminants rarely exert their effects through a single mechanism. Instead, they often induce a cascade of biological events involving oxidative stress, chronic inflammation, endocrine disruption, mitochondrial dysfunction, immune dysregulation, and genomic instability. These molecular disturbances eventually manifest as observable tissue lesions, such as cellular degeneration, necrosis, apoptosis, fibrosis, hyperplasia, dysplasia, and neoplasia [8].

For example, chronic PFAS exposure has been associated with hepatic steatosis and fibrosis, while microplastic accumulation has been linked to inflammatory responses and tissue remodeling in experimental models. Endocrine-disrupting chemicals have demonstrated the capacity to induce reproductive tissue abnormalities and developmental alterations, whereas pharmaceutical residues may contribute to organ-specific toxicity through prolonged low-dose exposure [25. Such pathological manifestations provide critical evidence connecting environmental exposure to adverse health outcomes [9].

Importantly, pathology offers an integrative perspective that complements environmental chemistry. Whereas environmental measurements quantify contaminant presence and exposure potential, pathological investigations reveal the biological consequences of those exposures. Histopathological endpoints therefore represent a crucial link between environmental contamination and disease manifestation.

1.4. Bridging Environmental Chemistry and Anatomic Pathology

Although environmental chemistry and anatomic pathology share a common interest in understanding disease causation, interactions between these disciplines remain relatively limited. Environmental chemists frequently investigate contaminant occurrence, environmental fate, and exposure pathways, whereas pathologists focus on tissue injury, disease progression, and lesion characterization [10]. The lack of integration between these fields has contributed to fragmented understanding of how environmental contaminants translate into clinically relevant pathological outcomes.

Establishing a bridge between environmental chemistry and anatomic pathology enables a more comprehensive assessment of environmental health risks. Such integration facilitates the identification of causal pathways linking contaminant exposure to tissue injury, supports the development of biologically relevant biomarkers, and enhances interpretation of toxicological findings.

Furthermore, pathological evidence can strengthen environmental risk assessments by providing direct indicators of adverse biological effects beyond conventional exposure measurements [11].

Emerging contaminants represent an ideal context for this interdisciplinary integration because their environmental occurrence is increasingly documented while their pathological implications remain incompletely understood [12]. Combining chemical characterization with histopathological evaluation allows researchers to trace the progression from environmental release and human exposure to molecular perturbation, cellular injury, tissue lesions, and ultimately organ dysfunction.

The convergence of environmental chemistry, toxicopathology, molecular pathology, and exposome science has given rise to the emerging concept of environmental pathology, a framework that seeks to understand disease processes through the lens of environmental exposures and tissue responses. This approach has significant implications for environmental health surveillance, disease prevention, regulatory decision-making, and public health policy.

1.5. Scope and Objectives

This review aims to comprehensively examine the environmental chemistry of major emerging contaminants and their implications for anatomic pathology. Specifically, the review focuses on microplastics, nanoplastics, PFAS, pharmaceutical residues, and endocrine-disrupting chemicals, which have emerged as priority contaminants due to their widespread distribution and potential health risks [13].

The objectives of this review are to: (I) summarize the environmental sources, occurrence, persistence, and transport of emerging contaminants; (II) examine major human exposure pathways and toxicokinetic processes; (III) evaluate molecular and cellular mechanisms underlying contaminant-induced toxicity; (IV) critically assess histopathological manifestations observed across major organ systems; (V) explore the relationship between chronic exposure and pathological progression toward organ dysfunction and carcinogenesis; and (VI) identify current knowledge gaps and future research priorities at the interface of environmental chemistry and anatomic pathology.

By integrating evidence from environmental sciences, toxicology, pathology, and biomedical research, this review seeks to provide a unified framework for understanding how emerging contaminants influence human health from molecular perturbation to tissue lesions and organ dysfunction.

2. ENVIRONMENTAL CHEMISTRY OF EMERGING CONTAMINANTS

Emerging contaminants comprise a heterogeneous group of anthropogenic substances that have gained increasing attention due to their widespread environmental occurrence, persistence, and potential impacts on ecological and human health [14]. Unlike conventional pollutants that have long been regulated and monitored, many emerging contaminants remain insufficiently characterized despite growing evidence of their environmental prevalence and biological activity. Advances in analytical chemistry have enabled the detection of these contaminants at increasingly lower concentrations, revealing their presence in air, water, soil, sediments, food products, wildlife, and human tissues [15].

The environmental behavior of emerging contaminants is governed by complex interactions involving physicochemical properties, environmental conditions, transport mechanisms, transformation pathways, and biological uptake processes. Understanding these characteristics is essential for evaluating exposure risks and predicting potential pathological consequences. Among the most concerning classes of emerging contaminants are microplastics and nanoplastics, per- and polyfluoroalkyl substances (PFAS), pharmaceutical residues, and endocrine-disrupting chemicals (EDCs), all of which demonstrate varying degrees of persistence, mobility, and bioaccumulation potential [16].

2.1. Microplastics and Nanoplastics

Microplastics (MPs), generally defined as plastic particles smaller than 5 mm, and nanoplastics (NPs), typically less than 1000 nm in size, have emerged as pervasive environmental contaminants with global distribution [17]. Their environmental significance stems not only from their abundance but also from their ability to interact with biological systems at cellular and molecular levels.

2.1.1. Sources and Environmental Occurrence

Microplastics originate from both primary and secondary sources. Primary microplastics are intentionally manufactured in microscopic sizes for industrial and commercial applications, including cosmetic products, personal care formulations, cleaning agents, and industrial abrasives [18]. Secondary microplastics arise from the degradation of larger plastic materials through physical, chemical, and biological weathering processes.

Major environmental sources include:

- Plastic packaging waste
- Tire wear particles generated during road transportation
- Synthetic textile fibers released during laundering
- Industrial discharges and manufacturing activities
- Fishing gear and marine debris
- Municipal wastewater effluents
- Agricultural plastic mulches and greenhouse materials

Recent studies have demonstrated the presence of microplastics in remote environments, including polar regions, deep-sea sediments, atmospheric aerosols, and mountain ecosystems, highlighting their remarkable environmental mobility [19].

2.1.2. Environmental Behavior and Transformation

The environmental behavior of microplastics is influenced by polymer composition, particle size, shape, density, surface charge, and weathering status. Once released into the environment, larger plastic materials undergo progressive fragmentation through ultraviolet radiation, mechanical abrasion, oxidation, hydrolysis, and microbial activity [19,20].

Fragmentation increases the formation of smaller particles with larger surface area-to-volume ratios, enhancing their reactivity and biological accessibility. Nanoplastics represent the terminal products of this degradation continuum and are particularly concerning because of their ability to cross biological membranes and accumulate within tissues [21].

2.1.3. Sorption and Transport of Pollutants

An important characteristic of microplastics is their ability to function as vectors for other environmental contaminants. Their hydrophobic surfaces readily adsorb pollutants including:

- Polycyclic aromatic hydrocarbons (PAHs)
- Polychlorinated biphenyls (PCBs)
- Heavy metals
- Pesticides
- Antibiotic residues

This phenomenon, often described as the "Trojan horse effect," may facilitate the transport of toxic substances into biological systems and potentially enhance toxicological outcomes [21,22].

2.1.4. Bioaccumulation Potential

Microplastics and nanoplastics have been detected in aquatic organisms, terrestrial animals, and human tissues, including blood, placenta, lungs, liver, and gastrointestinal samples. Their accumulation potential is strongly influenced by particle size, surface chemistry, and exposure duration. Nanoplastics exhibit greater translocation capacity than larger particles due to their nanoscale dimensions and increased cellular uptake potential [23].

2.2. Per- and Polyfluoroalkyl Substances (PFAS)

Per- and polyfluoroalkyl substances represent a large family of synthetic fluorinated compounds widely used in industrial applications and consumer products because of their exceptional thermal stability, water repellency, and chemical resistance [24].

2.2.1. Chemical Characteristics

PFAS are distinguished by the presence of multiple carbon-fluorine bonds, among the strongest covalent bonds in organic chemistry. This unique structural feature confers extraordinary environmental stability and resistance to degradation [24,25].

Common PFAS compounds include:

- Perfluorooctanoic acid (PFOA)
- Perfluorooctane sulfonate (PFOS)
- Perfluorohexane sulfonate (PFHxS)
- GenX chemicals
- Short-chain fluorinated alternatives

The remarkable bond strength between carbon and fluorine atoms significantly limits microbial degradation, photolysis, and hydrolysis processes, contributing to their designation as "forever chemicals".

2.2.2. Environmental Sources

Major environmental sources of PFAS include:

- Firefighting foams
- Non-stick cookware production
- Textile treatment industries
- Food packaging materials
- Electronics manufacturing
- Industrial wastewater discharges
- Landfill leachates

Environmental monitoring studies have documented PFAS contamination in surface waters, groundwater systems, marine environments, wildlife populations, and human biological samples worldwide [25].

2.2.3. Persistence and Environmental Mobility

PFAS exhibit exceptional persistence compared with most environmental contaminants. Their resistance to degradation allows long-range environmental transport and widespread distribution across ecosystems. Several PFAS compounds display substantial mobility in groundwater systems, increasing the risk of drinking-water contamination.

2.2.4. Bioaccumulation and Biomagnification

Unlike many hydrophobic pollutants that accumulate predominantly in fatty tissues, PFAS preferentially bind to proteins such as serum albumin and liver fatty acid-binding proteins. Consequently, elevated concentrations are often detected in the liver, kidneys, blood, and other highly perfused tissues. Long biological half-lives contribute to cumulative body burdens and prolonged internal exposure [26].

2.3. Pharmaceutical Residues

Pharmaceutical residues have emerged as important environmental contaminants due to increasing global consumption of medicinal products and incomplete removal during wastewater treatment processes [27]. Continuous release into aquatic and terrestrial environments has resulted in chronic, low-level exposure scenarios for both humans and wildlife.

2.3.1. Sources and Environmental Entry Pathways

Pharmaceutical contaminants enter environmental systems through multiple routes, including:

- Municipal wastewater effluents
- Hospital discharges
- Pharmaceutical manufacturing facilities
- Improper disposal of unused medications
- Agricultural use of veterinary drugs
- Aquaculture operations

Conventional wastewater treatment plants are often not designed to completely remove pharmaceutical compounds, facilitating their release into receiving water bodies.

2.3.2. Major Classes of Pharmaceutical Contaminants

- **Antibiotics**
  Antibiotics constitute one of the most extensively detected pharmaceutical groups in environmental matrices. Commonly identified compounds include sulfonamides, tetracyclines, fluoroquinolones, and macrolides. Environmental exposure to antibiotics may contribute to antimicrobial resistance development and alterations in microbial community structures.
- **Analgesics and Anti-inflammatory Drugs**
  Compounds such as ibuprofen, diclofenac, naproxen, and acetaminophen are frequently detected in wastewater and surface waters due to widespread consumption.
- **Hormonal Pharmaceuticals**
  Synthetic and natural hormones released through human excretion and pharmaceutical disposal can exert endocrine-disrupting effects even at trace concentrations.
- **Antidepressants and Neuroactive Compounds**
  Selective serotonin reuptake inhibitors (SSRIs) and related neuroactive substances are increasingly recognized as environmental contaminants capable of affecting aquatic organisms and potentially influencing neurobiological pathways.

2.3.3. Environmental Fate and Transformation

Pharmaceutical compounds undergo diverse transformation processes, including photolysis, biodegradation, hydrolysis, and oxidation. However, transformation products may retain biological activity and, in some cases, exhibit greater toxicity than their parent compounds. Consequently, environmental risk assessments increasingly consider both parent molecules and their metabolites [28].

2.4. Endocrine-Disrupting Chemicals

Endocrine-disrupting chemicals are exogenous substances capable of interfering with hormone synthesis, transport, metabolism, receptor binding, and physiological signaling pathway. Their widespread occurrence and biological potency have generated considerable concern regarding potential health effects [29].

2.4.1. Bisphenol A (BPA)

Bisphenol A is extensively used in the production of polycarbonate plastics and epoxy resins. Common sources include food packaging materials, beverage containers, thermal paper receipts, and consumer products.

Environmental release occurs through manufacturing processes, product degradation, landfill leachates, and wastewater effluents. BPA can mimic estrogenic activity and has been implicated in reproductive, developmental, metabolic, and carcinogenic effect [30].

2.4.2. Phthalates

Phthalates are plasticizers widely employed to improve flexibility and durability of polymeric materials. They are present in numerous products, including plastics, medical devices, personal care products, and construction materials.

Because phthalates are not chemically bound to polymer matrices, they are readily released into surrounding environments through volatilization, leaching, and abrasion processes [31].

2.4.3. Dioxins

Dioxins represent a group of highly persistent environmental pollutants generated primarily as by-products of industrial activities and combustion processes. These compounds exhibit strong lipophilicity, environmental persistence, and biomagnification potential, leading to accumulation within food chains [32].

2.4.4. Polychlorinated Biphenyls (PCBs)

Although banned in many countries, PCBs continue to persist in environmental reservoirs due to their chemical stability and resistance to degradation. Their persistence contributes to long-term contamination of soils, sediments, aquatic ecosystems, and biological tissues [33].

2.4.5. Environmental Persistence and Biological Relevance

Many endocrine disruptors exhibit prolonged environmental residence times and the ability to induce biological effects at extremely low concentrations. Their potential to interfere with hormonal regulation during critical developmental windows has raised concerns regarding reproductive disorders, developmental abnormalities, immune dysfunction, metabolic disease, and cancer susceptibility.

Collectively, endocrine-disrupting chemicals represent a unique class of emerging contaminants because their biological effects may occur independently of traditional dose-response assumptions, thereby challenging conventional toxicological paradigms [34].

Table 1. Major Emerging Contaminants and Their Environmental Characteristics.

Contaminant	Major Sources	Environmental Persistence	Bioaccumulation Potential
Microplastics	Plastic waste, packaging, textiles, tire wear	High	Moderate
Nanoplastics	Fragmentation of plastics	Very High	High
PFAS	Firefighting foams, industrial products, food packaging	Extremely High	Very High
BPA	Polycarbonate plastics, epoxy resins	Moderate	Moderate
Phthalates	Plasticizers, personal care products	Moderate	Moderate
PCBs	Legacy industrial equipment	Very High	Very High
Dioxins	Combustion and industrial by-products	Very High	Very High
Pharmaceutical Residues	Wastewater, hospitals, agriculture	Variable	Moderate
Antibiotics	Human and veterinary medicine	Variable	Moderate
Hormonal Drugs	Wastewater and pharmaceutical waste	Moderate	Moderate–High

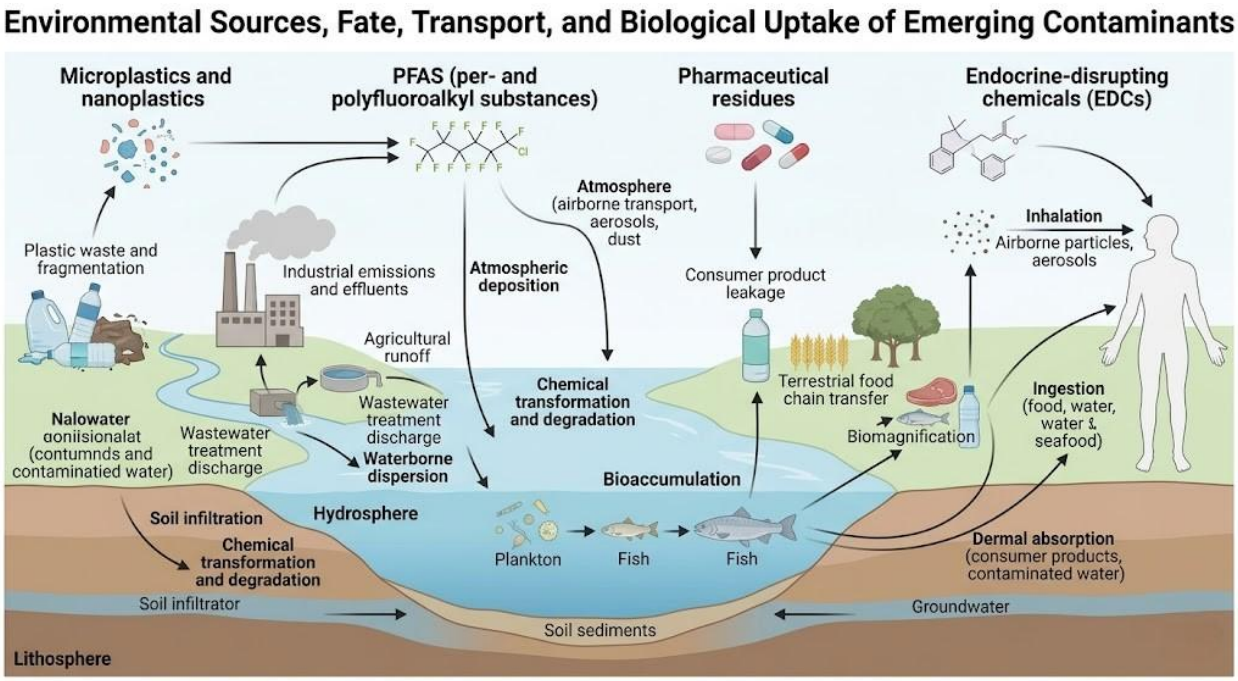


Figure 1. Environmental Sources, Fate, Transport, and Biological Uptake of Major Emerging Contaminants.

Schematic illustration showing the release of microplastics, PFAS, pharmaceutical residues, and endocrine-disrupting chemicals into environmental compartments (air, water, soil), their transport and transformation processes, bioaccumulation within food webs, and eventual human exposure through inhalation, ingestion, and dermal absorption pathways (**Figure1**).

3. HUMAN EXPOSURE AND TOXICOKINETIC PATHWAYS

The pathological consequences of emerging contaminants are largely determined by the extent and duration of exposure, as well as the toxicokinetic processes governing their absorption, distribution, metabolism, and excretion (ADME) within biological system. Human exposure to emerging contaminants occurs continuously through multiple environmental pathways, often involving simultaneous contact with diverse chemical mixtures [35]. Following entry into the body, contaminants may undergo transport, biotransformation, accumulation, and redistribution, ultimately reaching target organs where they can induce cellular and tissue damage.

Understanding exposure routes and toxicokinetic behavior is essential for elucidating how environmental contaminants progress from external environmental reservoirs to internal biological compartments. Emerging contaminants such as microplastics, nanoplastics, PFAS, pharmaceutical residues, and endocrine-disrupting chemicals exhibit distinct toxicokinetic profiles that influence their bioavailability, tissue distribution, and pathological outcomes [36].

3.1. Inhalation

Inhalation represents a major route of human exposure to numerous emerging contaminants, particularly airborne microplastics, nanoplastics, PFAS-containing particulates, industrial aerosols, and volatile endocrine-disrupting chemicals. Urbanization, industrialization, transportation activities, and indoor environmental conditions have significantly increased opportunities for respiratory exposure [37].

Airborne microplastics originate from multiple sources, including synthetic textile fibers, tire wear particles, household dust, construction materials, and industrial emissions. Due to their small size and low density, these particles can remain suspended in the atmosphere for prolonged periods and may be transported over considerable distances. Inhaled particles deposit within different regions of the respiratory tract depending on their aerodynamic properties.

Larger particles are typically retained within the upper respiratory tract, whereas smaller microplastics and nanoplastics may penetrate deeply into bronchioles and alveolar spaces. Once deposited, these particles can trigger local inflammatory responses, oxidative stress, epithelial injury, and macrophage activation. Experimental studies have demonstrated the translocation of nanosized particles across alveolar barriers into systemic circulation, thereby increasing the potential for extra-pulmonary effects [38].

PFAS and certain volatile endocrine disruptors may also enter the body through inhalation of contaminated dust and aerosols. Indoor environments often serve as important exposure settings because many consumer products continuously release chemical constituents into the surrounding air.

The respiratory system therefore functions not only as an exposure portal but also as a primary target organ for contaminant-induced pathology. Chronic inhalation exposure has been associated with airway inflammation, alveolar damage, pulmonary fibrosis, and impaired respiratory function in experimental models [39].

3.2. Ingestion

Ingestion is widely considered the dominant exposure route for many emerging contaminants owing to contamination of food, drinking water, and consumer products. Human populations are exposed daily through dietary intake, consumption of contaminated beverages, incidental ingestion of environmental particles, and transfer through food chains [40].

Microplastics and nanoplastics have been detected in bottled water, seafood, table salt, fruits, vegetables, milk products, and processed foods. Dietary exposure is further amplified by contamination arising from food packaging materials and food-processing equipment. Once ingested, a proportion of particles may be excreted, while smaller particles can penetrate gastrointestinal barriers and enter systemic circulation [41].

PFAS exposure frequently occurs through contaminated drinking water, fish, dairy products, meat, and agricultural produce. Due to their environmental persistence and biomagnification potential, PFAS concentrations may increase across trophic levels, resulting in elevated exposure among humans consuming contaminated food sources.

Pharmaceutical residues and endocrine-disrupting chemicals are similarly introduced through contaminated water supplies and food products. Wastewater reuse in agriculture and environmental contamination of aquatic ecosystems contribute to chronic low-level exposure scenarios.

Following gastrointestinal absorption, contaminants are transported via the portal circulation to the liver, which serves as a major site of metabolism and detoxification. Consequently, the digestive system represents both an important entry point and a critical determinant of systemic distribution.

3.3. Dermal Absorption

Although often considered less significant than inhalation and ingestion, dermal absorption can contribute substantially to total contaminant burden, particularly for endocrine-disrupting chemicals and PFAS-containing products. Human skin is routinely exposed to contaminants through contact with consumer products, occupational materials, contaminated water, soils, dust, and personal care products.

Bisphenol A, phthalates, and related endocrine-disrupting chemicals are commonly encountered in cosmetics, lotions, plastics, thermal paper receipts, and packaging materials. Repeated skin contact facilitates diffusion through the epidermal barrier, particularly when exposure is prolonged or when skin integrity is compromised [42].

PFAS-containing products such as waterproof textiles, stain-resistant coatings, and firefighting materials may also contribute to dermal exposure. While dermal absorption rates vary considerably among compounds, repeated low-dose exposure over extended periods may contribute meaningfully to cumulative body burdens.

Factors influencing dermal uptake include molecular size, lipophilicity, skin hydration, exposure duration, temperature, and individual physiological characteristics. Once absorbed, contaminants enter dermal capillaries and lymphatic vessels, facilitating systemic distribution to distant organs.

Although dermal absorption generally contributes less to overall exposure than ingestion, its importance should not be underestimated, especially in occupational settings and populations with frequent contact with contaminated materials [41-43].

3.4. Placental Transfer

Increasing evidence suggests that many emerging contaminants can cross the placental barrier and reach the developing fetus during critical stages of development. This finding has profound implications for developmental toxicology and environmental pathology because fetal tissues often exhibit heightened sensitivity to chemical insults.

Microplastics have been identified in placental tissues, amniotic fluid, and fetal membranes, indicating maternal-fetal transfer during pregnancy. Similarly, PFAS compounds readily cross the placenta owing to their protein-binding properties and systemic persistence. Numerous biomonitoring studies have reported detectable PFAS concentrations in umbilical cord blood and neonatal tissues [43].

Endocrine-disrupting chemicals such as BPA and phthalates also demonstrate placental permeability, raising concerns regarding developmental programming, reproductive abnormalities, neurodevelopmental alterations, and long-term disease susceptibility.

The placenta functions as a selective barrier rather than an absolute protective structure. Consequently, fetal exposure may occur even when maternal concentrations appear relatively low.

Prenatal exposure to emerging contaminants has been associated with altered immune function, impaired growth, endocrine disruption, metabolic disorders, and developmental abnormalities in both experimental and epidemiological studies [44].

The ability of contaminants to traverse placental barriers highlights the importance of considering vulnerable populations when evaluating environmental health risks.

3.5. Bioaccumulation and Organ Distribution

Following absorption, emerging contaminants undergo systemic distribution through blood circulation and may accumulate within specific tissues depending on their physicochemical properties, protein-binding affinity, lipid solubility, particle size, and biological persistence. Repeated exposure can result in progressive accumulation, increasing the likelihood of chronic toxicity and pathological injury [11,14].

Liver

The liver is one of the primary target organs for emerging contaminants because of its central role in xenobiotic metabolism and detoxification. PFAS, pharmaceutical residues, endocrine disruptors, and nanoplastics have all been detected within hepatic tissues. Accumulation may induce oxidative stress, inflammation, steatosis, fibrosis, and hepatocellular injury [34].

Kidney

The kidneys receive a substantial proportion of cardiac output and are therefore highly vulnerable to circulating contaminants. Renal accumulation is particularly relevant for PFAS due to active transport and reabsorption mechanisms. Chronic exposure has been associated with tubular degeneration, glomerular injury, impaired filtration, and nephrotoxicity [27-32].

Lung

The lungs serve both as a portal of entry and as a target organ for inhaled contaminants. Persistent deposition of microplastics, nanoplastics, and airborne chemicals can promote inflammatory responses, epithelial damage, alveolar remodeling, and pulmonary fibrosis. Nanoparticles may also enter systemic circulation following pulmonary absorption [30].

Brain

Emerging evidence indicates that certain contaminants possess the capacity to cross the blood-brain barrier and accumulate within neural tissues. Nanoplastics, PFAS, and some endocrine disruptors have been associated with neuroinflammation, oxidative stress, neurotransmitter disruption, and neuronal injury. Such effects raise concerns regarding cognitive dysfunction and neurodegenerative disease risk [45].

Reproductive Organs

The reproductive system is particularly susceptible to endocrine-active contaminants because of its dependence on tightly regulated hormonal signaling pathways. BPA, phthalates, PFAS, and related compounds have been detected in reproductive tissues and have been associated with impaired fertility, testicular degeneration, ovarian dysfunction, altered gametogenesis, and developmental abnormalities [41].

Factors Influencing Bioaccumulation

Several factors determine contaminant accumulation and organ distribution:

- Physicochemical properties of the contaminant
- Exposure concentration and duration
- Biological half-life
- Protein-binding affinity
- Lipophilicity
- Age and physiological status
- Genetic susceptibility
- Co-exposure to other contaminants

Collectively, these factors influence the internal dose delivered to target tissues and consequently determine the severity of pathological outcomes. Understanding organ-specific distribution patterns is therefore critical for interpreting histopathological findings and establishing mechanistic links between environmental exposure and disease development.

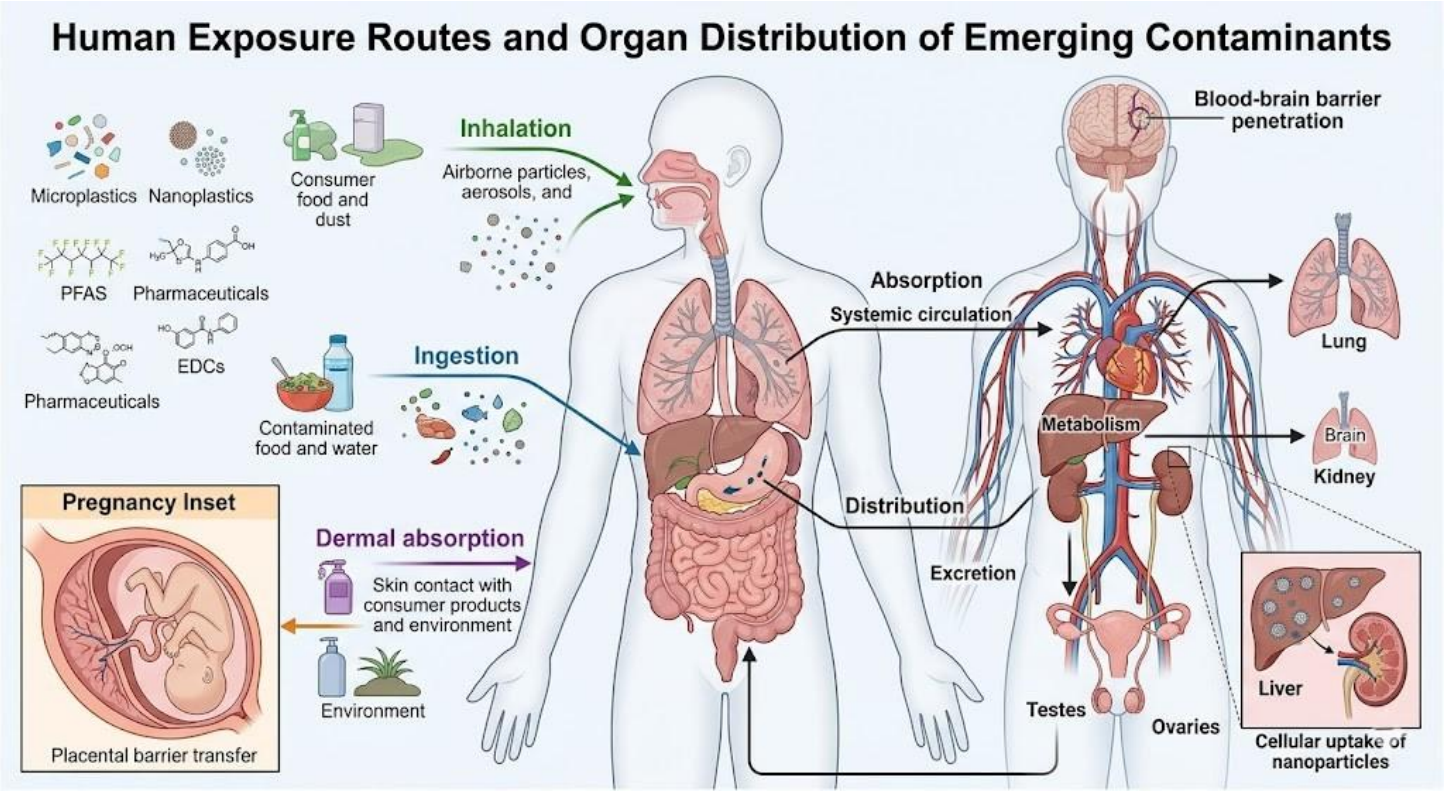


Figure 2. Human Exposure Routes and Organ Distribution of Emerging Contaminants

Conceptual illustration depicting major exposure pathways for emerging contaminants, including inhalation of airborne particles and aerosols, ingestion of contaminated food and water, dermal absorption from consumer products and environmental media, and maternal-fetal transfer across the placenta. The figure further illustrates systemic circulation, toxicokinetic processes (absorption, distribution, metabolism, and excretion), and preferential accumulation within target organs such as the liver, kidneys, lungs, brain, and reproductive tissues, where contaminant-induced pathological alterations may occur (**Figure 2**).

Table 2. Toxicokinetic Characteristics and Major Target Organs of Emerging Contaminants.

Contaminant Class	Major Exposure Route	Distribution Characteristics	Major Target Organs
Microplastics	Ingestion, inhalation	Gastrointestinal uptake, systemic transport	Gut, liver, lung
Nanoplastics	Ingestion, inhalation	Cross biological barriers	Brain, liver, placenta
PFAS	Drinking water, food	Strong protein binding	Liver, kidney, blood
BPA	Food packaging, dermal exposure	Rapid systemic distribution	Reproductive organs, liver
Phthalates	Dermal, ingestion	Lipid-associated distribution	Reproductive organs
Pharmaceutical Residues	Water, food	Organ-specific accumulation	Liver, kidney
Dioxins	Food chain	Fat tissue storage	Liver, immune organs
PCBs	Food chain	Bioaccumulation and biomagnification	Liver, nervous system

4. MOLECULAR AND CELLULAR MECHANISMS OF TOXICITY

The pathological consequences of emerging contaminants are mediated through a complex network of molecular and cellular events that ultimately culminate in tissue injury, organ dysfunction, and disease development. Although individual contaminants possess distinct physicochemical properties and biological behaviors, many converge on common toxicity pathways involving oxidative stress, inflammation, endocrine disruption, epigenetic dysregulation, and mitochondrial dysfunction [46]. These interconnected mechanisms form the biological foundation linking environmental exposure to histopathological alterations observed in target organs.

Increasing evidence suggests that chronic exposure to microplastics, nanoplastics, PFAS, pharmaceutical residues, and endocrine-disrupting chemicals can induce persistent cellular stress responses that overwhelm physiological defense mechanisms.

The resulting disturbances affect multiple cellular processes, including redox homeostasis, signal transduction, gene expression, energy metabolism, and programmed cell death pathways. Understanding these mechanisms is essential for elucidating the progression from environmental exposure to tissue lesions and organ pathology [47].

4.1. Oxidative Stress

Oxidative stress is one of the most extensively documented mechanisms underlying contaminant-induced toxicity and is considered a central event in the pathogenesis of many environmentally associated diseases [39]. It occurs when the generation of reactive oxygen species (ROS) exceeds the capacity of endogenous antioxidant defense systems, resulting in cellular and molecular damage.

4.1.1. Reactive Oxygen Species Generation

Emerging contaminants can stimulate ROS production through multiple pathways, including mitochondrial electron transport disruption, activation of oxidase enzymes, inflammatory cell recruitment, and redox cycling reactions. Common reactive oxygen species include:

- Superoxide anion ($O_2^{\bullet -}$)
- Hydrogen peroxide (H_2O_2)
- Hydroxyl radical ($\bullet OH$)
- Singlet oxygen ($^1O_2$)

Microplastics and nanoplastics can induce oxidative stress through direct interactions with cellular membranes and intracellular organelles, whereas PFAS exposure has been associated with enhanced ROS generation in hepatic and renal tissues. Pharmaceutical residues and endocrine disruptors similarly contribute to oxidative imbalance through interference with metabolic pathways and antioxidant systems [48].

Under physiological conditions, antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase maintain redox equilibrium. However, prolonged contaminant exposure may overwhelm these protective mechanisms, resulting in sustained oxidative injury.

4.1.2. Lipid Peroxidation

One of the primary consequences of excessive ROS production is lipid peroxidation, a process involving oxidative degradation of membrane lipids. Polyunsaturated fatty acids within cellular membranes are particularly susceptible to oxidative attack, leading to membrane instability and impaired cellular function.

Lipid peroxidation generates several reactive intermediates including:

- Malondialdehyde (MDA)
- 4-Hydroxynonenal (4-HNE)
- Lipid hydroperoxides

These products can further propagate oxidative damage and alter membrane permeability, ion transport, receptor function, and intracellular signaling pathways. Elevated levels of lipid peroxidation biomarkers have been reported following exposure to microplastics, PFAS, BPA, and various pharmaceutical contaminants [33].

4.1.3. DNA Damage

Reactive oxygen species can directly attack nucleic acids, producing a variety of DNA lesions, including strand breaks, base modifications, chromosomal abnormalities, and oxidative adduct formation. One of the most widely studied biomarkers of oxidative DNA damage is 8-hydroxy-2'-deoxyguanosine (8-OHdG) [24].

Persistent DNA damage may result in:

- Mutagenesis
- Genomic instability
- Altered gene expression
- Impaired DNA repair mechanisms
- Carcinogenic transformation

Experimental studies have demonstrated increased oxidative DNA damage following exposure to PFAS, nanoplastics, endocrine disruptors, and pharmaceutical residues, suggesting a potential mechanistic link between environmental contamination and carcinogenesis.

Collectively, oxidative stress serves as a critical initiating event that amplifies downstream pathological processes, including inflammation, fibrosis, apoptosis, and neoplastic transformation.

4.2. Chronic Inflammation

Inflammation is a fundamental biological response to injury and environmental stress. While acute inflammatory responses are generally protective, chronic inflammation can promote tissue damage, fibrosis, and disease progression. Numerous emerging contaminants have been shown to induce persistent inflammatory signaling pathways that contribute significantly to pathological outcomes.

4.2.1. NF-κB Activation

Nuclear factor kappa B (NF-κB) is a master transcription factor that regulates genes involved in immune responses, inflammation, cell survival, and stress adaptation. Activation of NF-κB represents a common cellular response to contaminant-induced oxidative stress and tissue injury.

Microplastics, PFAS, BPA, and various pharmaceutical residues have been shown to activate NF-κB signaling through mechanisms involving ROS generation, receptor-mediated pathways, and inflammatory mediators. Once activated, NF-κB translocates to the nucleus where it promotes the transcription of numerous pro-inflammatory genes [49].

Key downstream targets include:

- Tumor necrosis factor-alpha (TNF-α)
- Interleukin-1β (IL-1β)
- Interleukin-6 (IL-6)
- Cyclooxygenase-2 (COX-2)
- Inducible nitric oxide synthase (iNOS)

Sustained NF-κB activation may perpetuate inflammatory responses and contribute to chronic tissue injury.

4.2.2 Cytokine Release

Exposure to emerging contaminants frequently results in elevated production of pro-inflammatory cytokines and chemokines. These signaling molecules coordinate immune cell recruitment, amplify inflammatory responses, and influence tissue remodeling processes.

Commonly elevated inflammatory mediators include:

- TNF-α
- IL-1β
- IL-6
- IL-8
- Monocyte chemoattractant protein-1 (MCP-1)
- Transforming growth factor-beta (TGF-β)

Persistent cytokine production promotes leukocyte infiltration, extracellular matrix deposition, fibroblast activation, and progressive tissue remodeling. Such processes contribute directly to histopathological manifestations including chronic inflammation, fibrosis, epithelial hyperplasia, and organ dysfunction [44-46].

Chronic inflammation is increasingly recognized as a central mechanism linking environmental exposures to cancer development, metabolic disorders, neurodegenerative diseases, and reproductive dysfunction.

4.3. Endocrine Disruption

Many emerging contaminants possess endocrine-disrupting properties that interfere with normal hormonal regulation and cellular signaling. Because endocrine pathways govern growth, metabolism, reproduction, development, and immune function, disruption of these systems may have widespread pathological consequences [47].

4.3.1. Hormone Receptor Interference

Endocrine-disrupting chemicals can alter hormonal signaling through several mechanisms:

- Mimicking endogenous hormones
- Blocking hormone receptors
- Altering hormone synthesis
- Modifying hormone transport
- Disrupting hormone metabolism

Bisphenol A, phthalates, PFAS, and certain pharmaceutical residues have demonstrated the capacity to interact with estrogen, androgen, thyroid, glucocorticoid, and peroxisome proliferator-activated receptors (PPARs).

For example, BPA exhibits estrogenic activity by binding estrogen receptors and activating downstream signaling pathways even at low concentrations. Similarly, PFAS can influence lipid metabolism and endocrine regulation through interactions with PPAR signaling networks [45,49].

Hormonal dysregulation may result in:

- Reproductive abnormalities
- Developmental disorders
- Metabolic dysfunction
- Immune alterations
- Increased cancer susceptibility

Because endocrine signaling operates at extremely low physiological concentrations, even trace contaminant exposures may produce biologically significant effects.

4.4. Epigenetic Alterations

Epigenetic mechanisms regulate gene expression without altering underlying DNA sequences and are increasingly recognized as important mediators of environmentally induced diseases. Emerging contaminants can modify epigenetic programming, potentially resulting in persistent biological effects that extend beyond the initial exposure period.

4.4.1. DNA Methylation

DNA methylation involves the addition of methyl groups to cytosine residues, typically resulting in transcriptional repression. Environmental contaminants have been associated with both global and gene-specific methylation changes affecting pathways involved in:

- Cell proliferation
- Inflammation
- Metabolism

- Apoptosis
- Carcinogenesis

PFAS, BPA, phthalates, and pharmaceutical residues have been linked to altered methylation profiles in experimental and epidemiological studies. Such changes may contribute to developmental abnormalities, chronic disease susceptibility, and cancer risk [23-27].

4.4.2. Histone Modification

Histone proteins regulate chromatin structure and gene accessibility through post-translational modifications such as acetylation, methylation, phosphorylation, and ubiquitination. Environmental contaminants may disrupt these regulatory processes, leading to abnormal gene expression patterns [46].

Altered histone modifications have been implicated in:

- Inflammatory diseases
- Neurodevelopmental disorders
- Reproductive dysfunction
- Fibrotic diseases
- Tumor progression

Importantly, epigenetic alterations may persist long after exposure has ceased, raising concerns regarding transgenerational and long-term health effects.

4.5. Mitochondrial Dysfunction

Mitochondria are critical regulators of cellular energy production, redox balance, calcium homeostasis, and apoptosis. Increasing evidence indicates that mitochondria represent major intracellular targets of emerging contaminant toxicity.

4.5.1. ATP Depletion

Exposure to environmental contaminants may impair mitochondrial respiration by disrupting electron transport chain function and oxidative phosphorylation. Such impairment reduces adenosine triphosphate (ATP) production, compromising cellular energy availability [48].

Consequences of ATP depletion include:

- Impaired ion transport
- Reduced biosynthetic activity
- Cellular dysfunction
- Loss of membrane integrity
- Increased susceptibility to injury

Energy-demanding tissues such as the liver, kidneys, brain, and reproductive organs may be particularly vulnerable to mitochondrial impairment.

4.5.2. Apoptosis

Severe mitochondrial damage can initiate programmed cell death pathways through release of pro-apoptotic mediators, including cytochrome c and apoptosis-inducing factor. Activation of caspase-dependent and caspase-independent pathways ultimately leads to controlled cellular elimination.

While apoptosis serves an important physiological role in removing damaged cells, excessive activation may contribute to tissue degeneration and organ dysfunction. Persistent contaminant exposure may therefore result in cumulative cellular loss, impaired tissue regeneration, and progressive pathological alterations [49].

Mitochondrial dysfunction also amplifies oxidative stress and inflammatory signaling, creating a self-perpetuating cycle of cellular injury. Consequently, mitochondrial damage is increasingly regarded as a critical convergence point linking multiple mechanisms of emerging contaminant toxicity.

Overall, oxidative stress, chronic inflammation, endocrine disruption, epigenetic dysregulation, and mitochondrial dysfunction represent interconnected molecular pathways through which emerging contaminants exert toxic effects. These mechanisms collectively drive the development of tissue lesions and organ pathology discussed in subsequent sections of this review.

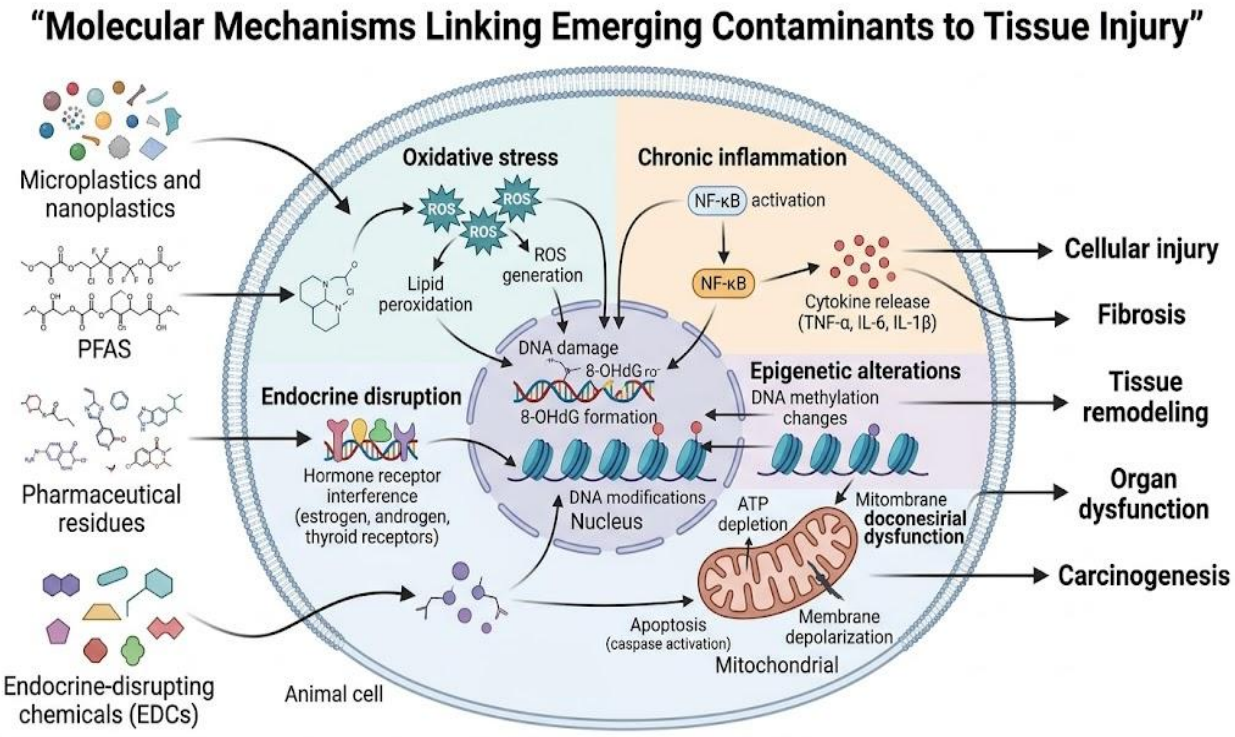


Figure 3. Molecular Mechanisms Linking Emerging Contaminants to Tissue Injury.

Schematic representation illustrating the principal molecular and cellular mechanisms through which emerging contaminants induce tissue damage. The figure should depict microplastics, nanoplastics, PFAS, pharmaceutical residues, and endocrine-disrupting chemicals triggering oxidative stress (ROS generation, lipid peroxidation, DNA damage), chronic inflammation (NF-κB activation, cytokine release), endocrine disruption (hormone receptor interference), epigenetic modifications (DNA methylation and histone alterations), and mitochondrial dysfunction (ATP depletion and apoptosis). These interconnected pathways converge to produce cellular injury, chronic inflammation, fibrosis, tissue remodeling, organ dysfunction, and carcinogenesis (**Figure 3)**.

Table 3. Molecular Mechanisms of Toxicity Associated with Emerging Contaminants.

Mechanism	**Key Cellular Events**	**Major Biomarkers**	**Potential Pathological Outcomes**
Oxidative Stress	ROS generation, antioxidant depletion	MDA, 8-OHdG, SOD, CAT	DNA damage, cellular degeneration
Chronic Inflammation	NF-κB activation, cytokine production	TNF-α, IL-1β, IL-6, CRP	Chronic inflammation, fibrosis
Endocrine Disruption	Hormone receptor interference	Estrogen receptor activity, thyroid hormones	Reproductive toxicity, developmental abnormalities
Epigenetic Alterations	DNA methylation, histone modification	Methylation markers, histone acetylation profiles	Aberrant gene expression, carcinogenesis
Mitochondrial Dysfunction	ATP depletion, membrane depolarization	ATP levels, cytochrome c, caspases	Apoptosis, organ dysfunction
Genotoxicity	DNA strand breaks, chromosomal damage	Comet assay, micronucleus formation	Mutagenesis, cancer initiation
Immune Dysregulation	Altered immune signaling	Cytokine profiles, immune cell markers	Autoimmune and inflammatory disorders

5. HISTOPATHOLOGICAL MANIFESTATIONS OF EMERGING CONTAMINANT EXPOSURE

The ultimate biological consequence of exposure to emerging contaminants is the development of structural and functional alterations at the tissue and organ levels. While molecular and cellular mechanisms such as oxidative stress, inflammation, endocrine disruption, and mitochondrial dysfunction provide mechanistic explanations, anatomic pathology offers direct morphological evidence of injury. Histopathological evaluation therefore represents a critical translational bridge between environmental exposure and clinical disease expression [43-45].

Across multiple organ systems, emerging contaminants induce a relatively conserved spectrum of lesions characterized by progressive cellular degeneration, inflammatory infiltration, tissue remodeling, and, in severe cases, neoplastic transformation. These changes are often chronic, low-grade, and cumulative, reflecting prolonged exposure to low environmental concentrations rather than acute toxic insults.

5.1. Liver Pathology

The liver is a principal target organ for emerging contaminants due to its central role in xenobiotic metabolism, detoxification, and systemic distribution of absorbed chemicals [122. Histopathological alterations observed in the liver following exposure to emerging contaminants include:

- Hepatic steatosis (fatty change)
- Hepatocellular degeneration
- Focal and centrilobular necrosis
- Portal and periportal inflammation
- Progressive fibrosis

Steatosis represents an early adaptive response to metabolic stress and lipid dysregulation, often progressing to inflammatory injury and fibrosis under sustained exposure conditions. PFAS, BPA, pharmaceuticals, and microplastics have all been associated with disruption of lipid metabolism and oxidative injury within hepatocytes [43,44].

5.2. Kidney Pathology

The kidney is highly vulnerable to circulating contaminants due to its extensive blood supply and concentrating function. Emerging contaminants accumulate within renal tubular cells and glomerular structures, leading to progressive nephrotoxicity.

Key histopathological features include:

- Tubular epithelial degeneration and vacuolization
- Glomerular basement membrane thickening
- Mesangial expansion
- Interstitial inflammation
- Tubulointerstitial fibrosis

PFAS and certain pharmaceuticals exhibit affinity for renal transport systems, contributing to prolonged retention and chronic injury. Nanoplastics may further exacerbate renal damage through oxidative stress and inflammatory responses within tubular epithelium [40].

5.3. Pulmonary Pathology

The lung serves as both an entry point and a primary target organ for airborne contaminants, particularly microplastics and nanoplastics. Repeated inhalation exposure results in persistent deposition within alveolar and interstitial compartments.

Histopathological manifestations include:

- Alveolar epithelial injury
- Chronic inflammatory infiltrates
- Interstitial thickening
- Granulomatous reactions
- Progressive interstitial fibrosis

These lesions reflect ongoing immune activation and impaired clearance mechanisms, particularly when particles escape macrophage-mediated degradation. Airborne PFAS and adsorbed toxicants on particulate matter may further intensify pulmonary injury [19,39].

5.4. Reproductive Toxicity

The reproductive system is highly sensitive to endocrine-active contaminants due to its dependence on tightly regulated hormonal signaling.

I. Male Reproductive Pathology

- Seminiferous tubule degeneration
- Reduced spermatogenic activity
- Leydig cell dysfunction
- Testicular atrophy

II. Female Reproductive Pathology

- Follicular atresia
- Ovarian stromal degeneration
- Disruption of folliculogenesis
- Hormonal imbalance-associated tissue remodeling

Bisphenol A, phthalates, and PFAS are strongly implicated in reproductive toxicity through estrogenic, anti-androgenic, and thyroid-disrupting mechanisms.

5.5. Neuropathology

Emerging contaminants are increasingly recognized as neurotoxic agents capable of crossing the blood-brain barrier, particularly in nanoparticle form.

Observed histopathological changes include:

- Neuroinflammation
- Microglial activation
- Neuronal degeneration
- Synaptic loss
- White matter alterations

Nanoplastics and PFAS have been associated with oxidative stress and inflammatory activation within neural tissues, potentially contributing to cognitive impairment and neurodegenerative disease processes.

Table 4. Histopathological Lesions Associated with Emerging Contaminant Exposure.

Organ System	Histopathological Lesions	Major Contaminants Implicated	Proposed Mechanisms
Liver	Steatosis, hepatocellular degeneration, necrosis, fibrosis, inflammatory infiltration	PFAS, BPA, microplastics, pharmaceuticals	Oxidative stress, mitochondrial dysfunction, lipid dysregulation, inflammation
Kidney	Tubular epithelial degeneration, glomerular injury, interstitial inflammation, fibrosis	PFAS, pharmaceuticals, nanoplastics	ROS generation, transporter-mediated accumulation, protein binding
Lung	Alveolar epithelial injury, chronic inflammation, granulomatous reactions, interstitial fibrosis	Microplastics, nanoplastics, airborne PFAS	Particle deposition, macrophage activation, chronic inflammation
Brain	Neuroinflammation, neuronal degeneration, microglial activation, synaptic loss	Nanoplastics, PFAS, BPA	Blood-brain barrier penetration, oxidative stress, immune activation
Testes	Seminiferous tubule degeneration, reduced spermatogenesis, Leydig cell dysfunction	BPA, phthalates, PFAS	Endocrine disruption, receptor-mediated toxicity
Ovary	Follicular atresia, ovarian stromal degeneration, impaired folliculogenesis	BPA, phthalates, PFAS	Hormonal imbalance, endocrine signaling disruption
Placenta	Vascular alterations, inflammatory infiltration, barrier dysfunction	Nanoplastics, PFAS	Transplacental transfer, oxidative injury

Immune Organs	Lymphoid depletion, immune dysregulation, altered immune cell populations	PFAS, dioxins, PCBs	Immunotoxicity, cytokine imbalance, receptor-mediated suppression

6. EMERGING CONTAMINANTS AND CARCINOGENIC POTENTIAL

A growing body of evidence suggests that chronic exposure to emerging contaminants may contribute to carcinogenesis through multifactorial pathways involving genotoxic injury, epigenetic reprogramming, sustained inflammatory signaling, and disruption of cellular homeostasis [45-50]. Although many emerging contaminants are not classical carcinogens in the traditional sense, their ability to induce long-term biological perturbations creates a permissive microenvironment for tumor initiation and progression.

Carcinogenesis in the context of environmental exposure is best understood as a multistep process involving initiation, promotion, and progression. Emerging contaminants may act at one or more of these stages through indirect mechanisms such as oxidative DNA damage, hormonal dysregulation, immune suppression, and chronic tissue injury. These processes collectively align with the hallmarks of cancer and provide a mechanistic framework linking environmental chemistry to oncologic pathology [51].

6.1. Genotoxicity

Genotoxicity represents one of the primary mechanisms by which environmental contaminants contribute to cancer development. It involves direct or indirect damage to DNA, leading to mutations, chromosomal instability, and impaired genomic integrity.

Emerging contaminants such as PFAS, nanoplastics, pharmaceutical residues, and endocrine-disrupting chemicals may induce genotoxic effects through several pathways:

- Reactive oxygen species (ROS)-mediated DNA strand breaks
- Formation of oxidative DNA adducts (e.g., 8-OHdG)
- Interference with DNA repair enzymes
- Chromosomal aberrations and micronucleus formation
- Replication stress and genomic instability

Nanoplastics, due to their ability to penetrate cellular and nuclear compartments, have been implicated in direct physical and oxidative DNA damage. Similarly, certain pharmaceuticals and industrial chemicals may undergo metabolic activation into reactive intermediates capable of binding DNA [50].

Persistent genotoxic stress increases the likelihood of somatic mutations in oncogenes and tumor suppressor genes, thereby initiating the carcinogenic cascade.

6.2. Epigenetic Dysregulation

Epigenetic alterations constitute a critical link between environmental exposure and long-term alterations in gene expression without changes in DNA sequence. Emerging contaminants can disrupt epigenetic regulation through DNA methylation changes, histone modifications, and dysregulation of non-coding RNAs.

6.2.1. DNA Methylation Alterations

Exposure to PFAS, BPA, and phthalates has been associated with global hypomethylation and gene-specific hypermethylation patterns affecting tumor-related genes. These modifications may lead to:

- Silencing of tumor suppressor genes
- Activation of oncogenic pathways
- Altered cellular differentiation
- Increased proliferative capacity

6.2.2. Histone and Chromatin Remodeling

Environmental contaminants may also influence histone acetylation and methylation states, thereby modifying chromatin accessibility and transcriptional activity. Such alterations can persist long after exposure cessation, contributing to sustained disease risk [52].

Epigenetic dysregulation is particularly significant because it may mediate transgenerational effects, potentially affecting offspring of exposed individuals.

6.3. Tumor Promotion

Tumor promotion refers to the selective expansion of initiated cells that have already acquired genetic damage. Emerging contaminants may act as tumor promoters by creating a tissue environment that favors survival, proliferation, and clonal expansion of altered cells.

Key promoting mechanisms include:

- Chronic inflammation and cytokine signaling (TNF-α, IL-6, IL-1β)
- Activation of NF-κB and STAT3 pathways
- Inhibition of apoptosis and enhanced cell survival
- Oxidative stress-induced adaptive proliferation
- Hormonal imbalance and endocrine disruption

For example, persistent inflammatory signaling induced by microplastics and PFAS exposure can lead to continuous tissue remodeling, fibrosis, and compensatory cell proliferation, increasing the probability of malignant transformation [53].

Tumor promotion is particularly important in environmentally relevant exposures, where low-dose but chronic exposure dominates rather than acute toxicity.

6.4. Disruption of Cancer Hallmarks

Emerging contaminants influence multiple biological processes that correspond to the established hallmarks of cancer, thereby contributing to a pro-oncogenic cellular phenotype.

- **Sustaining Proliferative Signaling**
  Endocrine disruptors such as BPA and phthalates can mimic hormonal signals, leading to sustained activation of growth pathways.
- **Evading Growth Suppressors**
  Epigenetic silencing of tumor suppressor genes may impair cell cycle checkpoints and apoptosis regulation.
- **Resisting Cell Death**
  Mitochondrial dysfunction and anti-apoptotic signaling induced by contaminants reduce programmed cell death.
- **Inducing Angiogenesis**
  Inflammatory cytokines such as VEGF may be upregulated in chronic exposure scenarios.
- **Activating Invasion and Metastasis**

  Chronic inflammation and extracellular matrix remodeling promote tissue invasion and metastatic potential.
- **Enabling Replicative Immortality**
  Persistent DNA damage and telomere instability may contribute to uncontrolled cellular replication.
- **Tumor-Promoting Microenvironment**
  Long-term inflammatory and oxidative stress environments support tumor progression.
  Collectively, these disruptions suggest that emerging contaminants do not act through a single oncogenic pathway but rather exert broad system-level effects that converge on malignant transformation.

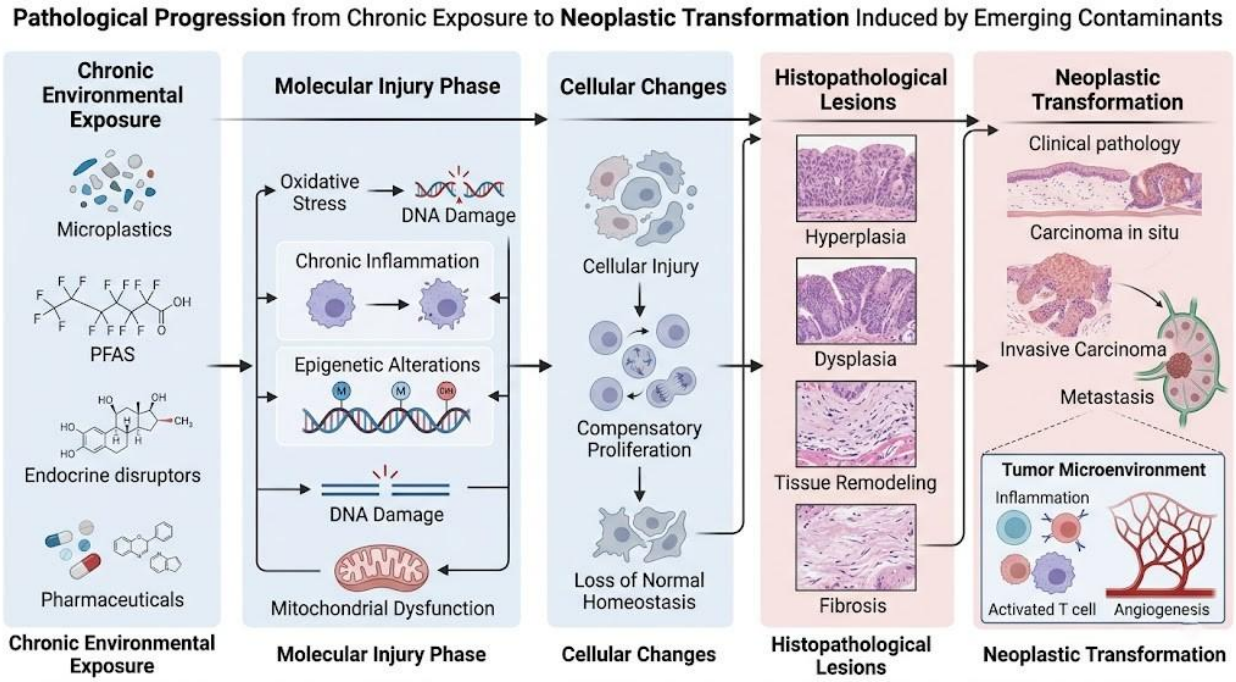


Figure 4. Pathological Progression from Chronic Exposure to Neoplastic Transformation.

The representation illustrating the progression from chronic exposure to emerging contaminants through molecular injury (oxidative stress, inflammation, endocrine disruption, epigenetic alterations, and mitochondrial dysfunction), leading to cellular damage, tissue remodeling, and histopathological changes (hyperplasia, dysplasia), ultimately progressing to carcinoma in situ and invasive cancer is shown in **Figure 4**. The figure emphasizes multistage carcinogenesis driven by environmental contaminants and highlights key molecular checkpoints involved in tumor initiation, promotion, and progression.

7. BIOMARKERS AND PATHOLOGICAL SURVEILLANCE

The translation of environmental exposure into clinically relevant disease outcomes requires reliable biomarkers that can capture both exposure burden and early biological effects. In the context of emerging contaminants, biomarker research spans traditional histopathological evaluation to advanced molecular and systems-level approaches. These tools are essential for linking environmental chemistry data with anatomic pathology findings and for improving early detection of contaminant-associated disease [54].

7.1. Histopathology

Histopathology remains the gold standard for the direct assessment of tissue injury and disease characterization. It provides morphological evidence of contaminant-induced damage, such as steatosis, fibrosis, necrosis, inflammatory infiltration, and cellular atypia.

Common histopathological techniques include:

- Hematoxylin and eosin (H&E) staining
- Special stains for fibrosis (Masson's trichrome)
- Lipid staining (Oil Red O)
- Immunohistochemical tissue profiling

In environmental pathology, histopathology serves as a definitive endpoint confirming that molecular and biochemical disturbances have progressed to structural tissue damage.

7.2. Immunohistochemistry

Immunohistochemistry (IHC) enables the localization and quantification of specific proteins within tissue sections, providing mechanistic insight into contaminant-induced pathology. It bridges the gap between molecular toxicology and morphological pathology.

Key IHC markers relevant to emerging contaminant exposure include:

- **Inflammatory markers:** TNF-α, IL-6, IL-1β
- **Oxidative stress markers:** 8-OHdG, Nrf2, HO-1
- **Apoptosis markers:** Caspase-3, BAX, BCL-2
- **Fibrosis markers:** α-SMA, TGF-β, collagen I
- **Proliferation markers:** Ki-67

These markers allow the identification of early tissue responses before overt histopathological damage becomes apparent.

7.3. Molecular Biomarkers

Molecular biomarkers provide quantitative measures of exposure and biological effect at the DNA, RNA, protein, and metabolite levels. They are particularly valuable in detecting subclinical changes induced by low-dose chronic exposure to emerging contaminants [55].

Common molecular biomarkers include:

- **DNA damage indicators:** 8-OHdG, comet assay parameters
- **Lipid peroxidation markers:** Malondialdehyde (MDA), 4-HNE
- **Inflammatory cytokines:** IL-6, TNF-α, CRP
- **Endocrine disruption markers:** hormone receptor levels, circulating hormones
- **Metabolic biomarkers:** altered lipid profiles, glucose dysregulation

Molecular biomarkers provide early warning signals of pathological processes before irreversible tissue damage occurs.

7.4. Omics Approaches

High-throughput omics technologies have transformed environmental health research by enabling comprehensive profiling of biological responses to contaminant exposure.

7.4.1. Genomics and Transcriptomics

Genomic and transcriptomic analyses reveal contaminant-induced changes in gene expression, mutation patterns, and regulatory networks. These approaches are essential for identifying pathways involved in carcinogenesis, inflammation, and metabolic disruption [56].

7.4.2. Proteomics

Proteomic profiling allows identification of altered protein expression and post-translational modifications associated with oxidative stress, inflammation, and cellular injury.

7.4.3. Metabolomics

Metabolomics provides insight into functional metabolic changes induced by contaminants, including disruptions in lipid metabolism, amino acid pathways, and energy production systems [55-57].

7.4.4. Integrated Multi-Omics

Integration of multi-omics datasets enables systems-level understanding of contaminant toxicity and supports the development of predictive models for disease outcomes.

8. KNOWLEDGE GAPS AND FUTURE PERSPECTIVES

Despite rapid advances in environmental chemistry and toxicology, significant gaps remain in understanding the full pathological implications of emerging contaminants. Addressing these gaps is essential for improving risk assessment and developing effective mitigation strategies [58,59].

8.1. Exposomics

Exposomics represents a comprehensive approach to characterizing the totality of environmental exposures across the human lifespan. It integrates chemical, biological, and environmental data to provide a holistic understanding of disease etiology.

Future research should focus on linking exposomic data with histopathological endpoints to establish direct exposure–disease correlations [60].

8.2. AI-Assisted Pathology

Artificial intelligence (AI) and machine learning are increasingly being applied to digital pathology for automated detection and classification of tissue abnormalities [61].

In environmental pathology, AI can enhance:

- Detection of subtle histological changes
- Quantification of fibrosis and inflammation
- Pattern recognition in large datasets
- Predictive modeling of disease progression

AI-assisted pathology has the potential to significantly improve the sensitivity and reproducibility of contaminant-related disease diagnosis.

8.3. Environmental Pathology

Environmental pathology is an emerging interdisciplinary field that integrates environmental science, toxicology, and anatomic pathology to understand disease processes driven by environmental exposures [62]. It emphasizes:

- Mechanistic linkage between exposure and tissue injury
- Integration of environmental and clinical data
- Development of exposure-informed diagnostic criteria

The establishment of environmental pathology as a formal discipline could significantly enhance the understanding of environmentally driven diseases [63].

8.4. One Health Approaches

The One Health framework recognizes the interconnectedness of human, animal, and environmental health [64]. Emerging contaminants affect all three domains simultaneously, making One Health approaches particularly relevant.

Future studies should integrate:

- Environmental monitoring
- Veterinary pathology
- Human clinical pathology
- Ecosystem-level assessments

Such integration will provide a more comprehensive understanding of contaminant impacts across biological systems [65].

9. CONCLUSIONS

Emerging contaminants represent a rapidly expanding class of environmental pollutants with significant implications for human health. This review demonstrates that microplastics, nanoplastics, PFAS, pharmaceutical residues, and endocrine-disrupting chemicals exert complex toxicological effects that extend from molecular perturbations to overt tissue and organ pathology.

By integrating environmental chemistry with anatomic pathology, a coherent framework emerges linking environmental exposure to oxidative stress, inflammation, endocrine disruption, epigenetic modifications, and mitochondrial dysfunction. These mechanisms converge to produce characteristic histopathological lesions across major organ systems, including the liver, kidneys, lungs, brain, and reproductive organs.

Furthermore, evidence suggests that chronic exposure to emerging contaminants may contribute to carcinogenesis through genotoxic, epigenetic, and tumor-promoting pathways. The incorporation of biomarker-based surveillance, histopathological assessment, and omics technologies provides powerful tools for early detection and mechanistic understanding of contaminant-induced disease.

Future progress in this field will depend on the integration of exposomics, AI-assisted pathology, and One Health frameworks to bridge remaining gaps between environmental exposure and disease manifestation. Ultimately, establishing environmental pathology as a unified discipline will enhance our ability to predict, diagnose, and mitigate the health impacts of emerging contaminants in a rapidly changing environment.

Acknowledgements

The authors appreciate the collaborative support of the Chemistry Collaborative Research Environment (CHEMCORE) for providing an enabling academic network for interdisciplinary research discussions and technical guidance during manuscript preparation.

Author Contributions

KSO conceptualized the study, developed the manuscript draft, provided overall supervision, literature review, chemical interpretation, and critical editing of the manuscript. OTA contributed specifically to histopathological components of the framework, clinical and anatomical pathology insights, and the critical interpretation of disease–pathology relationships. All authors reviewed, revised, and approved the final version of the manuscript.

Declaration of Competing Interests

The authors declare that they have no competing financial or non-financial interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of Generative AI and AI-Assisted Technologies

The authors declare that artificial intelligence tools (ChatGPT, OpenAI) were used only for language polishing and readability enhancement. No AI tools were used in the generation, analysis, or interpretation of scientific data. The authors retain full responsibility for the content of this manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

This study is a conceptual review and did not generate new experimental data. All information used in the manuscript was obtained from previously published studies, which are appropriately cited throughout the text.

Supplementary Information

No supplementary information is associated with this article.

Clinical Trial Registration

Not applicable.

References

[1] Kumar, P., Lata, K., Gacem, A., Khan, M. A., & Hanson, G. T. (2025). A review on the environmental fate, toxicological risks, and cutting-edge degradation methods of microplastics contamination. *Environmental Sciences Europe*, *37*, Article 114. https://doi.org/10.1186/s12302-025-01164-z

[2] Leslie, H. A., van Velzen, M. J. M., Brandsma, S. H., Vethaak, A. D., Garcia-Vallejo, J. J., & Lamoree, M. H. (2022). Discovery and quantification of plastic particle pollution in human blood. *Environment International*, *163*, Article 107199. https://doi.org/10.1016/j.envint.2022.107199

[3] Ullah, F., Wang, P. Y., Saqib, S., Zhao, L., Ashraf, M., Khan, A., Khan, W., Khan, A., Chen, Y., & Xiong, Y. C. (2025). Toxicological complexity of microplastics in terrestrial ecosystems. *iScience*, *28*(2), Article 111879. https://doi.org/10.1016/j.isci.2025.111879

[4] Ragusa, A., Svelato, A., Santacroce, C., Catalano, P., Notarstefano, V., Carnevali, O., Papa, F., Rongioletti, M. C. A., Baiocco, F., Draghi, S., D'Amore, E., Rinaldo, D., Matta, M., & Giorgini, E. (2021). Plasticenta: First evidence of microplastics in human placenta. *Environment International*, *146*, Article 106274. https://doi.org/10.1016/j.envint.2020.106274

[5] Lai, H., Liu, X., & Qu, M. (2022). Nanoplastics and human health: Hazard identification and biointerface. *Nanomaterials*, *12*(8), Article 1298. https://doi.org/10.3390/nano12081298

[6] Wang, H., Zhao, C., & Huo, T. (2025). The distribution of microplastic pollution and ecological risk assessment of Jingpo Lake—the world's second largest high-mountain barrier lake. *Biology*, *14*(2), Article 201. https://doi.org/10.3390/biology14020201

[7] Han, I., Lee, C., Belchez, C., Shipper, A. G., & Wiens, K. E. (2024). Microplastics in urban ambient air: A rapid review of active sampling and analytical methods for human risk assessment. *Environments*, *11*(11), Article 256. https://doi.org/10.3390/environments11110256

[8] Walker-Franklin, I., Villalobos Santeli, A., & Neal-Walthall, N. (2026). Tracking microplastics from source to impact: A review of environmental presence, exposure, remediation, and health risks. *Current Environmental Health Reports*, *13*(1), Article 12. https://doi.org/10.1007/s40572-026-00531-z

[9] Fenton, S. E., Ducatman, A., Boobis, A., DeWitt, J. C., Lau, C., Ng, C., Smith, J. S., & Roberts, S. M. (2021). Per- and polyfluoroalkyl substance toxicity and human health review: Current state of knowledge and strategies for informing future research. *Environmental Toxicology and Chemistry*, *40*(3), 606–630. https://doi.org/10.1002/etc.4890

[10] Okonji, K. S. (2025). Community perception of waterborne health risks in rocky-hill settlements of Nigeria: Implications for environmental justice and rural health policy in Sub-Saharan Africa. *Ethiopian Journal of Environmental Studies and Management*, *18*(4), 458–469. https://ejesm.org/doi/v18i4.3

[11] Alsadik, A., Akintunde, O. O., Habibi, H. R., & Achari, G. (2025). PFAS in water environments: recent progress and challenges in monitoring, toxicity, treatment technologies, and post-treatment toxicity. *Environmental Systems Research*, *14*(1), Article 18. https://doi.org/10.1186/s40068-025-00411-9

[12] Stem, A. D., Tieghi, R. S., Chatzi, V. L., Kleinstreuer, N., Valvi, D., Thompson, DC., & Vasiliou, V. (2025). Synergistic toxicity in alcohol-associated liver disease and PFAS exposure. *Toxicological Sciences*, *208*(1), 9–31. https://doi.org/10.1093/toxsci/kfaf110

[13] Rampazzo, G., Arioli, F., Pagliuca, G., Depau, G., Zironi, E., & Gazzotti, T. (2025). Cumulative exposure and health risk assessment of PFAS in animal-derived foods using the relative potency factor approach. *Toxics*, *13*(11), Article 931. https://doi.org/10.3390/toxics13110931

[14] Lee, J. C., Smaoui, S., Duffill, J., Marandi, B., & Varzakas, T. (2025). Research progress in current and emerging issues of PFASs' global impact: Long-term health effects and governance of food systems. *Foods*, *14*(6), Article 958. https://doi.org/10.3390/foods14060958

[15] Shittu, A. R., Iwaloye, O. F., Ojewole, E. A., Rabiu, A. G., Amechi, M. O., & Herve, O. F. (2023). The effects of per- and polyfluoroalkyl substances on environmental and human microorganisms and their potential for bioremediation. *Arhiv za Higijenu Rada i Toksikologiju*, *74*(3), 167–178. https://doi.org/10.2478/aiht-2023-74-3708

[16] Ahn, C., & Jeung, E. B. (2023). Endocrine-disrupting chemicals and disease endpoints. *International Journal of Molecular Sciences*, *24*(6), Article 5342. https://doi.org/10.3390/ijms24065342

[17] Lawal, F. O., & Okonji, K. S. (2025). Sub-threshold ecotoxicological risk of zinc, copper, and cadmium in soils near ceramic industrial zones: Implications for agricultural safety and environmental monitoring. *Journal of Materials and Environmental Science*, *16*(11), 2047–2058.

[18] Okon, M. B., Fasogbon, I. V., Swase, D., Dangana, R. S., Makena, W., Ojiakor, V. O., Etukudo, E. M., Chebet, J., Musyoka, A. M., Ifie, S. E., Mbyemeire, H., Mbina, S. A., Ugwu, O. P., Oviosun, A., Usman, I. M., Ifie, J. E., Rangasamy, L., Olorunnisola, O. S., Mounmbegna, P., Noreen, S., & Aja, P. M. (2025). Endocrine disruption rewards: bisphenol-A-induced reproductive toxicity and the precision ameliorative potential of flavonoids in preclinical studies. A systematic review and meta-analysis. *Frontiers in Toxicology*, *7*, Article 1687862. https://doi.org/10.3389/ftox.2025.1687862

[19] Wang, Y., & Qian, H. (2021). Phthalates and their impacts on human health. *Healthcare*, *9*(5), Article 603. https://doi.org/10.3390/healthcare9050603

[20] Barlas, T., Eroğlu Altinova, A., Coşkun, M., & Cerit, E. T. (2025). Endocrine disruptors, obesity, and metabolic syndrome. *Turkish Journal of Medical Sciences*, *55*(7), 1602–1612. https://doi.org/10.55730/1300-0144.6120

[21] Hilz, E. N., & Gore, A. C. (2023). Endocrine-disrupting chemicals: Science and policy. *Policy Insights from the Behavioral and Brain Sciences*, *10*(2), 142–150. https://doi.org/10.1177/23727322231196794

[22] Breese, N. M., Truong, L., Li, X., Tanguay, R. L., & Lehmler, H.-J. (2026). Morphological, behavioral, and transcriptomic profiling reveals developmental toxicity of PCB metabolites in zebrafish. *Toxics*, *14*(5), Article 444. https://doi.org/10.3390/toxics14050444

[23] aus der Beek, T., Weber, F. A., Bergmann, A., Hickmann, S., Ebert, I., Hein, A., & Küster, A. (2016). Pharmaceuticals in the environment—Global occurrences and perspectives. *Environmental Toxicology and Chemistry*, *35*(4), 823–835. https://doi.org/10.1002/etc.3339

[24] Larsson, D. G. J., & Flach, C. F. (2022). Antibiotic resistance in the environment. *Nature Reviews Microbiology*, *20*(5), 257–269. https://doi.org/10.1038/s41579-021-00649-x

[25] Islam, I. U., Qurashi, A. N., Adnan, A., Ahmed, S., & Malik, M. A. (2025). Bioremediation and adsorption: Strategies for managing pharmaceutical pollution in aquatic environment. *Water, Air, & Soil Pollution*, *236*, Article 579. https://doi.org/10.1007/s11270-025-08193-7

[26] Wilkinson, J. L., Boxall, A. B. A., Kolpin, D. W., Leung, K. M. Y., Lai, R. W. S., Galbán-Malagón, C., et al. (2022). Pharmaceutical pollution of the world's rivers. *Proceedings of the National Academy of Sciences*, *119*(8), Article e2113947119. https://doi.org/10.1073/pnas.2113947119

[27] Ojija, F. (2024). Emerging environmental contaminants: Sources, effects on biodiversity and humans, remediation, and conservation implications. *Science Progress*, *107*(2), Article 00368504241253720. https://doi.org/10.1177/00368504241253720

[28] Sule, R. O., Rivera, G. D. T., Vaidya, T., Gartrell, E., & Gomes, A. V. (2025). Environmental toxins and oxidative stress: The link to cardiovascular diseases. *Antioxidants*, *14*(5), Article 604. https://doi.org/10.3390/antiox14050604

[29] Mao, H., Zhao, X., & Sun, S. (2025). NF-κB in inflammation and cancer. *Cellular & Molecular Immunology*, *22*, 811–839. https://doi.org/10.1038/s41423-025-01310-w

[30] Zuo, M., Ye, M., Lin, H., Liao, S., Xing, X., Liu, J., Wu, D., Huang, Z., & Ren, X. (2024). Mitochondrial dysfunction in environmental toxicology: Mechanisms, impacts, and health implications. *Chemical Research in Toxicology*, *37*(11), 1794–1806. https://doi.org/10.1021/acs.chemrestox.4c00328

[31] Klibaner-Schiff, E., Simonin, M. E., Akdis, C. A., Cheong, A., Johnson, M. M., Karagas, M. R., Kirsh, S., Kline, O., Mazumdar, M., Oken, E., Sampath, V., Vogler, N., Wang, X., & Nadeau, K. C. (2024). Environmental exposures influence multigenerational epigenetic transmission. *Clinical Epigenetics*, *16*(1), Article 145. https://doi.org/10.1186/s13148-024-01762-3

[32] Kadac-Czapska, K., Ośko, J., Knez, E., & Grembecka, M. (2024). Microplastics and oxidative stress—Current problems and prospects. *Antioxidants*, *13*(5), Article 579. https://doi.org/10.3390/antiox13050579

[33] Cheng, Y. F., Zhao, Y. J., Chen, C., & Zhang, F. (2025). Heavy metals toxicity: Mechanism, health effects, and therapeutic interventions. *MedComm*, *6*(9), Article e70241. https://doi.org/10.1002/mco2.70241

[34] Beier, J. I., Luo, J., Vanderpuye, C. M., Brizendine, P., Muddasani, P., Bolatimi, O., Heinig, S. A., Ekuban, F. A., Siddiqui, H., Ekuban, A., Gripshover, T. C., Wahlang, B., Watson, W. H., & Cave, M. C. (2025). Environmental pollutants, occupational exposures, and liver disease. *Seminars in Liver Disease*, *45*(2), 148–166. https://doi.org/10.1055/a-2540-2861

[35] Lawal, F. O., & Okonji, K. S. (2025). Trace metals concentration in soils around a ceramic factory, Ajaokuta, Kogi State, Nigeria. *Journal of Applied Sciences and Environmental Management*, *29*(9), 315–319. https://doi.org/10.4314/jasem.v29i9.74

[36] Tripathy, D. B., Pradhan, S., Gupta, A., & Agarwal, P. (2025). Nanoparticles induced neurotoxicity. *Nanotoxicology*, *19*(3), 325–352. https://doi.org/10.1080/17435390.2025.2488310

[37] Lee, S. E., & Park, Y. S. (2026). Environmental pollution and its impact on kidney diseases: A comprehensive review of current evidence. *Life*, *16*(2), Article 291. https://doi.org/10.3390/life16020291

[38] Dzierżyński, E., Gawlik, P. J., Puźniak, D., Flieger, W., Jóźwik, K., Teresiński, G., Forma, A., Wdowiak, P., Baj, J., & Flieger, J. (2024). Microplastics in the human body: Exposure, detection, and risk of carcinogenesis: A state-of-the-art review. *Cancers*, *16*(21), Article 3703. https://doi.org/10.3390/cancers16213703

[39] Dutta, S., Sengupta, P., Bagchi, S., Chhikara, B. S., Pavlík, A., Sláma, P., & Roychoudhury, S. (2023). Reproductive toxicity of combined effects of endocrine disruptors on human reproduction. *Frontiers in Cell and Developmental Biology*, *11Trace*, Article 1162015. https://doi.org/10.3389/fcell.2023.1162015

[40] Wan, D., Liu, Y., Chang, Q., Liu, Z., Wang, Q., Niu, R., Gao, B., Guan, Q., & Xia, Y. (2024). Micro/nanoplastic exposure on placental health and adverse pregnancy risks: Novel assessment system based upon targeted risk assessment environmental chemicals strategy. *Toxics*, *12*(8), Article 553. https://doi.org/10.3390/toxics12080553

[41] Daramola, A. O., Folaranmi, O. E., & Okonji, K. S. (2026). Chemical exposure, self-reported haematological symptoms, and laboratory safety practices among undergraduate and postgraduate science and medical students. *Nigerian Research Journal of Chemical Sciences*, *14*(1), 298–311.

[42] Guillien, A., Ghosh, M., Gille, T., & Dumas, O. (2023). The exposome concept: how has it changed our understanding of environmental causes of chronic respiratory diseases? *Breathe*, *19*(2), Article 230044. https://doi.org/10.1183/20734735.0044-2023

[43] Zhu, G., Wen, Y., Cao, K., He, S., & Wang, T. (2024). A review of common statistical methods for dealing with multiple pollutant mixtures and multiple exposures. *Frontiers in Public Health*, *12*, Article 1377685. https://doi.org/10.3389/fpubh.2024.1377685

[44] Kim, W. W., Zarus, G., Alman, B., Ruiz, P., Han, M., Mehta, P., Ji, C., Qureshi, H., Antonini, J., & Shoeb, M. (2025). Metal-induced genotoxic events: Possible distinction between sporadic and familial ALS. *Toxics*, *13*(6), Article 493. https://doi.org/10.3390/toxics13060493

[45] Miller, G. W., & Banbury Exposomics Consortium. (2025). Integrating exposomics into biomedicine. *Science*, *388*(6745), 356–358. https://doi.org/10.1126/science.adr0544

[46] Chatziioannou, A. C., Myridakis, A., & Stephanou, E. G. (2025). Biomonitoring of environmental phenols, phthalate metabolites, triclosan, and per- and polyfluoroalkyl substances in humans with chromatography and mass spectrometry. *Toxics*, *13*(12), Article 1029. https://doi.org/10.3390/toxics13121029

[47] Fuller, R., Landrigan, P. J., Balakrishnan, K., Bathan, G., Bose-O'Reilly, S., Brauer, M., Caravanos, J., Chiles, T., Cohen, A., Corra, L., Cropper, M., Ferraro, G., Hanna, J., Hanrahan, D., Hu, H., Hunter, D., Janata, G., Kupka, R., Lanphear, B., . . . Yan, C. (2022). Pollution and health: a progress update. *The Lancet Planetary Health*, *6*(6), e535–e547. https://doi.org/10.1016/S2542-5196(22)00090-0

[48] Niehoff, N. M., Goldberg, M., & White, A. J. (2022). The importance of addressing early life environmental exposures in cancer epidemiology. *Current Epidemiology Reports*, *9*, 49–65. https://doi.org/10.1007/s40471-022-00289-6

[49] Folaranmi, O. E., Okonji, K. S., Lawal, F. O., & Lawal, G. F. (2026). Environmental contaminants, microbial dysbiosis, and hematological disorders: From soil and water to the bloodstream. *Journal of Materials and Environmental Science*, *17*(5), 828–865.

[50] Lawal, F. O., & Okonji, K. S. (2026). Heavy metal contamination of soils in industrial ceramic sites with long-term ecological and sustainable land use implications. *Journal of Environmental Spectrum*, *6*(1), 27–36. https://doi.org/10.66567/t9wndc22

[51] Okonji, K. S. (2025). Environmental impacts of industrial activities on soil and water quality: A comprehensive review. *International Journal of Engineering Sciences & Research Technology*, *14*(12), 14–25. https://doi.org/10.29121/ijesrtp.v14.i12.2025.2

[52] Mafe, A. N., & Büsselberg, D. (2026). Cancer and environmental xenobiotics: Mechanisms, controversies, and innovations. *Journal of Xenobiotics*, *16*(1), Article 2. https://doi.org/10.3390/jox16010002

[53] Wogan, G. N., Hecht, S. S., Felton, J. S., Conney, A. H., & Loeb, L. A. (2004). Environmental and chemical carcinogenesis. *Seminars in Cancer Biology*, *14*(6), 473–486. https://doi.org/10.1016/j.semcancer.2004.06.010

[54] Weinstein, I. B., Arcoleo, J., Lambert, M., Hsiao, W., Gattoni-Celli, S., Jeffrey, AM., & Kirschmeier, P. (1985). Mechanisms of multistage chemical carcinogenesis and their relevance to respiratory tract cancer. *Carcinogenesis: A Comprehensive Survey*, *8*, 395–409.

[55] Czaczkowska, L., Jabłońska, E., & Ratajczak-Wrona, W. (2025). Endocrine disruptors and breast cancer: A comprehensive review. *Biomedicines*, *13*(11), Article 2774. https://doi.org/10.3390/biomedicines13112774

[56] Singh, D. D. (2025). Epigenetic mechanisms of endocrine-disrupting chemicals in breast cancer and their impact on dietary intake. *Journal of Xenobiotics*, *15*(1), Article 1. https://doi.org/10.3390/jox15010001

[57] Mafe, A. N., & Büsselberg, D. (2025). Cancer and environmental xenobiotics: Mechanisms, controversies, and innovations. *Journal of Xenobiotics*, *16*(1), Article 2. https://doi.org/10.3390/jox16010002

[58] Seyyedsalehi, M. S., & Boffetta, P. (2023). Per- and poly-fluoroalkyl substances (PFAS) exposure and risk of kidney, liver, and testicular cancers: A systematic review and meta-analysis. *La Medicina del Lavoro*, *114*(5), Article e2023040. https://doi.org/10.23749/mdl.v114i5.15065

[59] Ponce-Cusi, R., Barletta-Carrillo, C., & Pilco-Ferreto, N. (2025). Microplastics and nanoplastics in cancer progression: Biology and public health. *Biomedicines*, *14*(1), Article 1. https://doi.org/10.3390/biomedicines14010001

[60] Zhang, A., Luo, X., Li, Y., Yan, L., Lai, X., Yang, Q., Zhao, Z., Huang, G., Li, Z., Wu, Q., & Wang, J. (2024). Epigenetic changes driven by environmental pollutants in lung carcinogenesis: a comprehensive review. *Frontiers in Public Health*, *12*, Article 1420933. https://doi.org/10.3389/fpubh.2024.1420933

[61] Krajka-Kuźniak, V., Belka, M., & Papierska, K. (2024). Targeting STAT3 and NF-κB signaling pathways in cancer prevention and treatment: The role of chalcones. *Cancers*, *16*(6), Article 1092. https://doi.org/10.3390/cancers16061092

[62] National Toxicology Program. (2023). *NTP technical report on the toxicology and carcinogenesis studies of perfluorooctanoic acid (CASRN 335-67-1) administered in feed to Sprague Dawley (Hsd:Sprague Dawley® SD®) rats* (Revised; Technical Report 598). National Institutes of Health. https://doi.org/10.22427/NTP-TR-598

[63] Dlamini, Z., Alaouna, M., Marutha, T., Mkhize-Kwitshana, Z., Mbodi, L., Chauke-Malinga, N., Luvhengo, T. E., Marima, R., Hull, R., Skepu, A., Ntwasa, M., Duarte, R., Damane, B. P., Mosoane, B., Mbatha, S., Phakathi, B., Khaba, M., Chokwe, R. C., Edge, J., . . . Molefi, T. (2025). The exposome perspective: Environmental and infectious agents as drivers of cancer disparities in low- and middle-income countries. *Cancers*, *17*(15), Article 2537. https://doi.org/10.3390/cancers17152537

[64] Fakhri, K. U., Sharma, D., Fatma, H., Yasin, D., Alam, M., Sami, N., Ahmad, F. J., Shamsi, A., & Rizvi, M. A. (2025). The dual role of dietary phytochemicals in oxidative stress: Implications for oncogenesis, cancer chemoprevention, and ncRNA regulation. *Antioxidants*, *14*(6), Article 620. https://doi.org/10.3390/antiox14060620

[65] Jomova, K., Alomar, S. Y., Valko, R., Fresser, L., Nepovimova, E., Kuca, K., & Valko, M. (2026). Interplay of oxidative stress and antioxidant mechanisms in cancer development and progression. *Archives of Toxicology*, *100*(1), 27–73. https://doi.org/10.1007/s00204-025-04146-5