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Environmental Contaminants, Microbial Dysbiosis, and Hematological Disorders: From Soil and Water to the Bloodstream

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Abstract: Environmental contamination of soil and water by heavy metals, pesticides, pharmaceuticals, petroleum derivatives, and emerging pollutants represents a major global health burden. Beyond direct toxicological effects, growing evidence indicates that these contaminants exert systemic impacts through complex interactions involving microbial dysbiosis, antimicrobial resistance selection, bioaccumulation, and multi-organ dysfunction. After environmental exposure, toxicants enter plants, animals, and humans through ingestion, inhalation, and dermal absorption, ultimately accumulating in the bloodstream where they interact with plasma proteins, erythrocytes, leukocytes, and bone marrow compartments. Contaminant-induced alterations of soil and aquatic microbiota promote reduced microbial diversity and enhance the proliferation of resistant and opportunistic pathogens. These polluted environments function as reservoirs for antimicrobial resistance genes and infectious agents capable of entering human and animal hosts. In parallel, exposure to environmental toxicants disrupts gut microbial balance, increases intestinal permeability, and facilitates endotoxin translocation, triggering systemic inflammatory responses. Elevated pro-inflammatory cytokines, oxidative stress, and iron sequestration mechanisms collectively impair erythropoiesis and hematological stability. Mechanistically, heavy metals inhibit heme synthesis, induce reactive oxygen species formation, damage hematopoietic stem cells, and suppress bone marrow function. Pharmaceuticals and pesticides further contribute to immune dysregulation and organ toxicity, particularly affecting hepatic and renal systems that regulate detoxification and erythropoietin production. Epidemiological and experimental findings increasingly associate chronic environmental exposure with anemia, leukocyte abnormalities, thrombocytopenia, leukemia, lymphoma, and sepsis-related hematologic complications in both humans and animals. This review integrates environmental toxicology, microbiology, immunology, and hematology into a unified framework describing an environmental–microbial–immune–organ axis of haematotoxicity. It highlights key biomarkers for exposure assessment and identifies research gaps necessary for advancing risk evaluation and One Health–based environmental policies.

1. Introduction

Rapid industrialization, urban expansion, intensive agriculture, mining activities, petroleum exploitation, pharmaceutical manufacturing, and improper waste disposal have significantly increased the release of environmental contaminants into soil and aquatic ecosystems worldwide (Landrigan *et al.*, 2020; UNEP, 2022). These pollutants include heavy metals, pesticides, polycyclic

aromatic hydrocarbons (PAHs), pharmaceuticals, endocrine-disrupting chemicals, and microplastics, all of which persist in environmental matrices and accumulate through trophic transfer in food chains. Unlike biodegradable organic compounds, heavy metals such as lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) remain chemically stable and bioavailable for prolonged periods, posing long-term health risks to humans and animals (Jaishankar *et al.*, 2021; El Hammari *et al.*, 2022). Traditionally, environmental toxicology research has focused on direct organ toxicity, particularly hepatic and renal damage. However, emerging evidence suggests that the bloodstream represents a central interface where environmental contaminants exert systemic biological effects. Toxicants enter the body through ingestion of contaminated food and water, inhalation of polluted air, and dermal absorption, after which they bind to plasma proteins, erythrocytes, and immune cells, facilitating systemic distribution (Kim *et al.*, 2022). Accumulation in circulating blood and bone marrow compartments interferes with erythropoiesis, leukocyte maturation, and platelet production, ultimately contributing to hematological disorders.

Increasing attention has also shifted toward the role of environmental contaminants in disrupting microbial ecosystems. Polluted soils and aquatic systems exhibit reduced microbial diversity and altered community composition, often characterized by the enrichment of metal-resistant bacteria and the co-selection of antimicrobial resistance (AMR) genes (Chen *et al.*, 2022; Singh *et al.*, 2023). These contaminated environments act as reservoirs for resistant pathogens and mobile genetic elements that can be transmitted to humans and animals through environmental exposure and food consumption. The propagation of AMR within polluted ecosystems amplifies infection risks and complicates treatment outcomes. Beyond environmental microbiota, contaminants significantly affect the human gut microbiome. Experimental and epidemiological studies demonstrate that heavy metals, pesticides, and pharmaceutical residues alter microbial community structure, reduce beneficial commensal populations, and increase intestinal permeability (Liu *et al.*, 2022). Microbiome disruption enhances lipopolysaccharide (LPS) translocation into systemic circulation, activating toll-like receptor 4 (TLR4) signaling pathways and inducing pro-inflammatory cytokine production such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α). Chronic inflammatory activation suppresses erythropoietin signaling and disrupts iron homeostasis, contributing to anemia of inflammation and other hematological abnormalities (Weiss and Ganz, 2021). Hepatic and renal systems further mediate contaminant-induced hematotoxicity. The liver plays a central role in detoxification and xenobiotic metabolism, while the kidneys regulate waste excretion and erythropoietin production. Persistent exposure to toxicants induces oxidative stress, mitochondrial dysfunction, and inflammatory injury in these organs, thereby impairing their regulatory functions and exacerbating blood-related abnormalities (Chen *et al.*, 2022). Renal dysfunction reduces erythropoietin synthesis, whereas hepatic impairment alters iron metabolism and coagulation pathways, collectively influencing hematological stability. Importantly, environmental contamination affects not only humans but also animals and wildlife. Livestock and aquatic organisms bioaccumulate toxicants from contaminated feed, water, and soil, leading to measurable alterations in blood indices and immune responses. These changes have implications for food safety and zoonotic transmission of resistant microorganisms, reinforcing the need for a One Health perspective that integrates environmental, animal, and human health systems. Despite growing evidence linking environmental contamination to systemic inflammation and organ toxicity, limited studies have comprehensively integrated microbial dysbiosis, bioaccumulation, bloodstream toxicant dynamics, and hematological disorders into a unified mechanistic framework (Karim *et al.*, 2016).

Most existing research addresses these domains independently rather than examining their interconnected pathways. Therefore, this review aims to synthesize current literature (2010–2026) to elucidate how environmental contaminants:

i. Alter microbial ecosystems and promote antimicrobial resistance,

ii. Bioaccumulate and enter systemic circulation,

iii. Induce liver and kidney dysfunction,

iv. Trigger immune-mediated inflammation, and

v. Contribute to hematological disorders in humans and animals.

By integrating environmental toxicology, microbiology, and hematology, this work proposes an environmental–microbial–immune–organ axis model of hematotoxicity and identifies key research gaps for future investigation.

2. Sources of Environmental Contaminants

Environmental contaminants that contribute to hematotoxicity originate from multiple anthropogenic and natural activities. Rapid industrial growth, mining operations, agricultural intensification, pharmaceutical manufacturing, petroleum exploitation, urbanization, and improper waste management have collectively intensified the release of toxic substances into soil, water, and atmospheric systems (Landrigan *et al.*, 2020; UNEP, 2022, Okonji, 2025). These contaminants persist in environmental compartments, undergo transformation by microbial and chemical processes, and enter food chains through bioaccumulation and trophic transfer.

2.1 Heavy Metals from Industrial and Mining Activities

Heavy metals including lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) remain among the most extensively studied hematotoxic contaminants (Lawal and Okonji, 2025). Mining, smelting, battery recycling, ceramic production, oil drilling, and industrial effluent discharge represent major sources of metal contamination in soil and groundwater systems (Jaishankar *et al.*, 2021). Similar contamination patterns and ecological concerns have also been reported in sediment systems associated with effluent discharge in Nigeria (Abubakar *et al.*, 2025). Unlike organic pollutants, heavy metals are non-biodegradable and persist indefinitely in environmental matrices. They bind strongly to soil particles but remain bioavailable under acidic or disturbed conditions, increasing plant uptake and groundwater contamination. Crops cultivated in contaminated soils accumulate metals in edible tissues, creating a direct exposure pathway for humans and livestock (Lawal and Okonji, 2025). Epidemiological evidence demonstrates that chronic exposure to lead and cadmium correlates with reduced hemoglobin levels, impaired erythropoiesis, and increased risk of hematological malignancies (Zhang *et al.*, 2021). Mechanistically, lead interferes with heme synthesis by inhibiting δ-aminolevulinic acid dehydratase (ALAD), whereas cadmium induces oxidative stress and disrupts hematopoietic stem cell proliferation.

2.2 Agricultural Runoff and Pesticide Contamination

Modern agricultural systems rely heavily on synthetic pesticides, including organophosphates, carbamates, organochlorines, and neonicotinoids. Improper application and runoff transport these compounds into nearby rivers, groundwater, and surrounding ecosystems (Tang *et al.*, 2020). Pesticides exhibit immunotoxic and hematotoxic properties through oxidative stress induction,

mitochondrial dysfunction, and disruption of immune cell signaling. Chronic exposure has been associated with leukocyte abnormalities, altered platelet function, and increased risk of hematologic disorders (Mostafalou and Abdollahi, 2020). Beyond direct toxicity, pesticides alter soil microbial communities and reduce beneficial bacteria populations. This microbial shift influences nutrient cycling and promotes ecological imbalance, indirectly affecting contaminant mobility and bioavailability.

2.3 Pharmaceutical Residues and Wastewater Effluents

Pharmaceutical compounds, including antibiotics, analgesics, anti-inflammatory drugs, and endocrine-disrupting chemicals, are increasingly detected in wastewater systems and surface waters worldwide (aus der Beek *et al.*, 2016; Wilkinson *et al.*, 2022). Municipal sewage treatment plants often fail to completely remove pharmaceutical residues, allowing these compounds to persist in aquatic environments. Antibiotics in wastewater promote selective pressure for antimicrobial resistance (AMR) among environmental bacteria, facilitating horizontal gene transfer and the expansion of resistance gene pools (Chen *et al.*, 2022).

From a hematological perspective, pharmaceutical contaminants can:

a. Alter immune cell regulation

b. Induce inflammatory responses

c. Disrupt hormonal control of hematopoiesis

d. Contribute to chronic systemic toxicity

2.4 Petroleum Derivatives and Polycyclic Aromatic Hydrocarbons (PAHs)

Petroleum extraction, oil spills, combustion processes, and industrial emissions release polycyclic aromatic hydrocarbons (PAHs) into the environment. Benzo[a]pyrene is among the most toxic PAHs and is frequently detected in contaminated soil and water systems. PAHs bind to the aryl hydrocarbon receptor (AhR), activating xenobiotic metabolism pathways and generating reactive metabolites that form DNA adducts. Such genotoxic interactions increase the risk of hematological malignancies, including leukemia and lymphoma (Smith *et al.*, 2020). Oil-contaminated regions often demonstrate elevated blood abnormalities among exposed populations, reflecting systemic absorption of hydrocarbon derivatives.

2.5 Microplastics as Emerging Contaminants

Microplastics originate from plastic degradation, synthetic textile fibers, tire wear, and urban waste. These particles accumulate in aquatic ecosystems and agricultural soils, where they adsorb heavy metals, pesticides, and organic pollutants (**Table1**). Recent studies indicate that microplastics can translocate across intestinal barriers and enter systemic circulation, triggering inflammatory responses and oxidative stress (Shen *et al.*, 2021). Their role as pollutant carriers enhances co-exposure to toxic substances, compounding hematological risk.

3. Toxicokinetics: From Environmental Exposure to Bloodstream

Environmental contaminants exert hematological effects only after successful absorption, systemic distribution, and interaction with target organs. Toxicokinetics describes the processes of absorption, distribution, metabolism, and excretion (ADME), which determine internal dose and biological impact (ATSDR, 2020). In contaminated ecosystems, toxicants are ingested through food

and water, inhaled as airborne particles, or absorbed through dermal contact. Once absorbed, they enter the bloodstream, where they bind to plasma proteins, erythrocytes, or circulating lipids and are transported to organs including the liver, kidneys, bone marrow, and spleen. (**Figure 1**). These contaminants persist in environmental compartments, undergo transformation by microbial and chemical processes, and enter food chains through bioaccumulation and trophic transfer (Ebong and Bassey, 2025).

Table 1. Major Environmental Contaminants and Their Primary Sources

Contaminant Class	Examples	Major Environmental Sources	Persistence	Hematological Relevance
Heavy metals	Pb, Cd, As, Hg	Mining, industrial effluents, oil spills	Non-degradable	Anemia, marrow suppression
Pesticides	Organophosphates, organochlorines	Agricultural runoff	Moderate–High	Leukocyte dysfunction
PAHs	Benzo[a]pyrene	Petroleum combustion	High	DNA damage, leukemia risk
Pharmaceuticals	Antibiotics, NSAIDs	Wastewater effluent	Emerging	Immune dysregulation
Microplastics	Polyethylene fragments	Urban waste, plastics	Persistent	Inflammation, toxic carrier

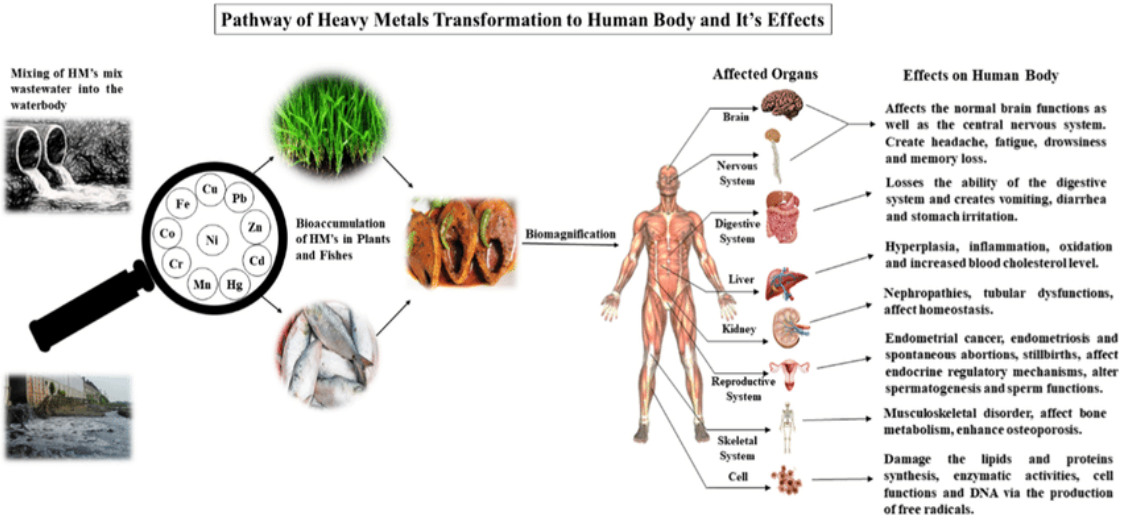

Figure 1. Mechanistic Pathway of Heavy Metals into the food chain and then to the human body. https://link.springer.com/article/10.1007/s11356-022-22122-9?utm

3.1 Routes of Exposure and Systemic Absorption

3.1.1 Ingestion

The ingestion of contaminated crops, livestock products, drinking water, or seafood represents the primary exposure pathway for heavy metals, pesticides, pharmaceutical residues, and microplastics. Heavy metals are absorbed in the gastrointestinal tract via metal transporter proteins

that normally regulate essential elements such as iron and zinc. For example, cadmium competes with zinc transport pathways, facilitating its systemic absorption (Jaishankar *et al.*, 2021). Pharmaceutical residues and pesticides are absorbed across intestinal epithelial cells and may undergo partial hepatic metabolism before systemic distribution.

3.1.2 Inhalation

Airborne particulate matter generated from industrial emissions, mining dust, combustion processes, and waste incineration contains adsorbed heavy metals and organic pollutants. Inhaled particles deposit in alveolar spaces and diffuse into pulmonary capillaries, entering systemic circulation directly. This bypasses first-pass hepatic metabolism, increasing bioavailability and systemic toxicity (Landrigan *et al.*, 2020).

3.1.3 Dermal Absorption

Certain lipophilic contaminants, including organochlorine pesticides and PAHs, penetrate skin barriers and enter systemic circulation via dermal diffusion. Occupational exposure significantly increases this risk among agricultural and industrial workers.

3.2 Transport in Blood and Bioavailability

Once contaminants enter circulation, they bind to:

i. Albumin

ii. Transferrin

iii. Hemoglobin

iv. Lipoproteins

Heavy metals such as lead and arsenic demonstrate affinity for erythrocytes and plasma proteins, enabling prolonged blood retention. Blood concentration levels therefore serve as biomarkers of exposure. Persistent circulation increases the likelihood of toxicant deposition in:

a. Bone marrow

b. Liver

c. Kidneys

d. Immune tissues

3.3 Bioaccumulation in Organs Relevant to Hematology

3.3.1 Liver

The liver metabolizes xenobiotics through phase I and phase II detoxification pathways. However, chronic exposure overwhelms detoxification capacity, leading to oxidative stress, mitochondrial dysfunction, and inflammatory injury. Hepatic impairment disrupts:

a. Iron metabolism

b. Coagulation factor synthesis

c. Plasma protein production

These disruptions indirectly influence hematological stability.

3.3.2 Kidneys

Kidneys regulate:

i. Waste excretion

ii. Electrolyte balance

iii. Erythropoietin production

Toxicant-induced renal injury reduces erythropoietin synthesis, leading to impaired red blood cell production and anemia (Chen *et al.*, 2022). Cadmium and arsenic accumulate in renal tubular cells, promoting tubular dysfunction and chronic kidney disease, which further exacerbates hematological impairment.

3.3.3 Bone Marrow

Bone marrow is highly sensitive to oxidative stress and inflammatory signaling. Toxicants that accumulate in marrow niches interfere with:

a. Hematopoietic stem cell proliferation

b. Differentiation into erythroid and myeloid lineages

Benzene metabolites are particularly damaging to hematopoietic progenitor cells and are strongly associated with aplastic anemia and leukemia development (Smith *et al.*, 2020).

3.4 Pharmacokinetic Interaction with the Microbiome

Emerging research demonstrates that gut microbiota influence toxicant metabolism. Microbial enzymes may:

i. Biotransform heavy metals

ii. Modify pesticide metabolites

iii. Influence pharmaceutical degradation

Conversely, contaminants alter microbial composition, reducing beneficial species and promoting resistant organisms (Liu *et al.*, 2022). Thus, toxicokinetics is not solely a chemical process but a biologically interactive system mediated by microbiota, (**Table 2**).

Table 2. Toxicokinetic Pathways from Environment to Bloodstream

Exposure Route	Absorption Mechanism	Blood Transport	Primary Target Organs	Hematological Impact
Ingestion	Intestinal transport proteins	Albumin-bound	Liver, bone marrow	Anemia, marrow suppression
Inhalation	Alveolar diffusion	Direct plasma entry	Kidneys, immune tissue	Leukocyte dysfunction
Dermal	Lipophilic diffusion	Systemic circulation	Peripheral tissues	Chronic inflammation
Trophic transfer	Bioaccumulation	Persistent blood exposure	Multi-organ	Long-term toxicity

These contaminants persist in environmental compartments, undergo transformation by microbial and chemical processes, and enter food chains through bioaccumulation and trophic transfer (Gain *et al.*, 2025).

4. Environmental Microbiology Dimension

Environmental contaminants do not remain chemically isolated after deposition in soil and aquatic systems. Instead, they interact dynamically with microbial communities, altering microbial diversity, metabolic activity, gene expression patterns, and horizontal gene transfer rates. Polluted ecosystems increasingly function as evolutionary hotspots where antimicrobial resistance (AMR) genes, virulence factors, and contaminant-adapted microbial communities co-evolve under strong selective pressure (Chen *et al.*, 2022; Singh *et al.*, 2023). These microbial shifts create a biological bridge between environmental pollution and systemic human and animal diseases. Importantly, microbial alterations influence not only infection risk but also inflammatory signaling pathways that contribute to hematological dysfunction.

4.1 Soil Microbial Alteration Under Heavy Metal Stress

Heavy metals such as lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) exert persistent selective pressure on soil microbial communities. Unlike organic pollutants, heavy metals are non-degradable and accumulate in soil matrices, maintaining long-term ecological toxicity. Studies demonstrate that metal-contaminated soils exhibit:

a. Significant reductions in microbial alpha diversity

b. Shifts in bacterial community composition toward resistant taxa

c. Increased abundance of stress-response genes

d. Enhanced expression of metal efflux transport systems

e. Elevated horizontal gene transfer activity

Heavy metal exposure induces microbial adaptation mechanisms including efflux pumps, sequestration proteins, enzymatic detoxification, and biofilm formation. However, these resistance determinants are frequently encoded on mobile genetic elements that co-localize with antibiotic resistance genes. This co-localization results in **co-selection**, where exposure to metals indirectly selects for antibiotic-resistant bacteria even in the absence of antibiotic pressure (Chen *et al.*, 2022). Mechanistically, plasmids, transposons, and integrons facilitate gene transfer among microbial populations in contaminated soils. As a result, polluted agricultural land becomes a reservoir for multidrug-resistant organisms that can be transmitted through:

i. Crop consumption

ii. Livestock feeding

iii. Surface runoff into water systems

From a hematological perspective, the clinical risk arises when resistant pathogens or their endotoxins enter the bloodstream, triggering inflammatory cascades that impair bone marrow function and red blood cell production.

4.2 Co-Selection of Antimicrobial Resistance in Polluted Environments

Environmental pollution accelerates antimicrobial resistance expansion through selective pressure mechanisms that operate independently of clinical antibiotic misuse. Pollutants that promote AMR include:

a. Heavy metals

b. Residual antibiotics from wastewater

c. Disinfectants

d. Industrial chemicals

e. Pesticides

These contaminants create survival advantages for bacteria harboring resistance determinants. Horizontal gene transfer plays a central role in this process. Resistance genes are exchanged via:

i. Conjugative plasmids

ii. Transduction by bacteriophages

iii. Transformation of extracellular DNA

iv. Integron-mediated gene capture

Studies show that contaminated wastewater and industrial effluents contain high concentrations of multidrug-resistant bacteria such as:

a) *Escherichia coli*

b) *Klebsiella pneumoniae*

c) *Pseudomonas spp.*

d) *Vibrio spp.*

These organisms possess virulence factors and resistance genes that increase infection severity and reduce treatment efficacy. The public health implication is critical: when such pathogens infect humans or animals, they may lead to systemic infections requiring prolonged antibiotic treatment (Okonji and Dash, 2026). Persistent infections induce chronic inflammatory responses that directly affect hematopoiesis by suppressing erythroid progenitor cell activity. Thus, polluted environments serve as ecological incubators for resistant pathogens that contribute indirectly to hematological impairment.

4.3 Environmental Pathogens and Bloodstream Infections

Contaminated aquatic environments frequently harbor opportunistic pathogens capable of invading systemic circulation. Major risk sources include:

i. Untreated wastewater discharge

ii. Floodwater contamination

iii. Agricultural runoff

iv. Recreational water exposure

These environments contain elevated loads of Gram-negative bacteria and endotoxin-producing organisms. When pathogenic bacteria breach epithelial barriers through ingestion wounds, gastrointestinal compromise, or skin injury, they can enter the bloodstream and trigger bacteremia. Systemic dissemination of pathogens leads to:

a. Sepsis

b. Hemolysis

c. Disseminated intravascular coagulation (DIC)

d. Leukocyte exhaustion

e. Platelet consumption

Sepsis represents a particularly important hematological complication because it causes dysregulated immune activation followed by immune suppression. Sepsis-associated inflammation suppresses hematopoietic stem cell proliferation and alters iron metabolism through increased hepcidin production. This contributes to anemia of inflammation and abnormal leukocyte profiles. Therefore, environmental pathogen exposure constitutes a direct microbial pathway linking pollution to blood disorders.

4.4 Gut Microbiome Disruption After Environmental Exposure

Environmental contaminants ingested through contaminated food and water exert profound effects on intestinal microbial ecosystems. Experimental and human studies demonstrate that heavy metals, pesticides, and pharmaceutical residues:

i. Reduce beneficial commensal bacteria

ii. Increase opportunistic pathogen abundance

iii. Disrupt microbial metabolic pathways

iv. Alter short-chain fatty acid production

v. Increase intestinal epithelial permeability

Such alterations lead to dysbiosis, defined as an imbalance between protective and pathogenic microbial populations. One of the most critical consequences of dysbiosis is increased translocation of lipopolysaccharide (LPS) from Gram-negative bacteria into systemic circulation. LPS activates Toll-like receptor 4 (TLR4), initiating signaling cascades that stimulate production of:

a. Interleukin-6 (IL-6)

b. Tumor necrosis factor-α (TNF-α)

c. C-reactive protein (CRP)

d. Chronic activation of these inflammatory mediators results in:

e. Hepcidin upregulation

f. Iron sequestration within macrophages

g. Suppression of erythropoietin signaling

h. Reduced red blood cell synthesis

This pathway explains how microbiome disruption directly contributes to anemia of chronic inflammation and impaired hematological stability (Liu *et al.*, 2022). Thus, the gut microbiome functions as a biological mediator between environmental exposure and blood pathology.

4.5 Environmental Microbiome as a Reservoir of Haematotoxic Risk

Polluted ecosystems act as convergence zones where:

i. Resistance genes accumulate

ii. Virulence factors proliferate

iii. Toxicant-adapted microbial communities evolve

These ecosystems continuously recycle genetic elements that enhance microbial survival under contaminant pressure. From a public health perspective, this creates a sustained exposure pathway:

Environmental contamination

→ Microbial adaptation

→ Resistance expansion

→ Pathogen transmission

→ Systemic infection

→ Hematological dysfunction

Repeated microbial-induced inflammatory activation contributes to:

a. Chronic anemia

b. Leukocyte dysregulation

c. Platelet dysfunction

d. Increased infection susceptibility

Thus, environmental microbiomes are not passive ecological components, they actively modulate systemic hematological risk, (**Table 3**).

Table 3. Microbial Mediation of Environmental Hematological Effects

Environmental Factor	Microbial Effect	Immune Response	Hematological Outcome
Heavy metals	Reduced diversity, resistant strains	Chronic inflammation	Anemia
Antibiotics in water	AMR gene expansion	Persistent infections	Leukocyte dysfunction
Wastewater pathogens	Pathogen proliferation	Sepsis activation	Hemolysis
Pesticides	Microbiome imbalance	Cytokine release	Bone marrow suppression

5. Mechanisms of Hematotoxicity

Environmental contaminants exert hematological toxicity through multiple overlapping mechanisms involving oxidative stress, disruption of heme synthesis, immune activation, genotoxicity, and organ dysfunction. These mechanisms operate independently and synergistically, amplifying systemic damage in exposed populations. Importantly, hematotoxicity is not limited to direct chemical interference with blood cells. It is mediated through:

i. Toxicant–cell interactions

ii. Microbial inflammation

iii. Hepatic and renal dysfunction

iv. Cytokine-mediated suppression of hematopoiesis

Understanding these pathways provides mechanistic plausibility linking environmental contamination to blood disorders.

5.1 Inhibition of Heme Synthesis and Iron Metabolism Disruption

One of the most established mechanisms of heavy metal–induced hematotoxicity is interference with heme biosynthesis. Lead (Pb) inhibits δ-aminolevulinic acid dehydratase (ALAD), an essential enzyme in the heme synthesis pathway. Inhibition of ALAD results in accumulation of δ-aminolevulinic acid and reduced hemoglobin production, leading to microcytic anemia (Jaishankar *et al.,* 2021). Arsenic and cadmium also disrupt iron utilization and interfere with enzymatic processes involved in erythropoiesis. Beyond direct enzymatic inhibition, inflammatory cytokines induced by microbial dysbiosis stimulate hepcidin production in the liver. Hepcidin reduces iron export from macrophages and intestinal epithelial cells, resulting in iron sequestration and anemia of inflammation (Weiss and Ganz, 2021). Thus, hematological impairment arises from both:

i. Direct toxic inhibition of heme synthesis

ii. Immune-mediated iron restriction

5.2 Oxidative Stress and Reactive Oxygen Species (ROS) Generation

A central pathway linking environmental contaminants to blood damage is oxidative stress. Heavy metals, pesticides, pharmaceuticals, and hydrocarbons promote excessive production of reactive oxygen species (ROS) within:

a. Erythrocytes

b. Leukocytes

c. Bone marrow cells

ROS induce lipid peroxidation of red blood cell membranes, reducing membrane stability and increasing hemolysis risk. Red blood cells are particularly vulnerable because they lack nuclei and have limited antioxidant repair mechanisms. Experimental studies demonstrate that chronic exposure to cadmium and arsenic significantly increases malondialdehyde (MDA) levels, a biomarker of oxidative damage, while reducing antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (Chen *et al.,* 2022). Persistent oxidative stress damages hematopoietic stem cells and impairs differentiation into mature blood cell lineages.

5.3 Genotoxicity and Hematopoietic Stem Cell Damage

Several environmental contaminants exert genotoxic effects that directly affect bone marrow progenitor cells. Benzene metabolites are particularly toxic to hematopoietic stem cells. They form DNA adducts, induce chromosomal aberrations, and interfere with cell cycle regulation (Smith *et al.*, 2020).

Similarly:

i. PAHs generate reactive intermediates that bind DNA

ii. Arsenic induces genomic instability

iii. Heavy metals interfere with DNA repair enzymes

iv. Accumulation of DNA damage in hematopoietic stem cells increases the risk of:

v. Aplastic anemia

vi. Myelodysplastic syndromes

vii. Leukemia development

Thus, long-term exposure creates a carcinogenic and hematotoxic risk profile.

5.4 Cytokine-Mediated Bone Marrow Suppression

Microbial dysbiosis and bloodstream infections induce chronic inflammatory signaling. Activation of Toll-like receptors (especially TLR4 via LPS) stimulates production of pro-inflammatory cytokines including:

a. Interleukin-6 (IL-6)

b. Tumor necrosis factor-α (TNF-α)

c. Interleukin-1β (IL-1β)

These cytokines suppress bone marrow activity by:

i. Inhibiting erythroid progenitor proliferation

ii. Disrupting hematopoietic stem cell niche signaling

iii. Reducing erythropoietin sensitivity

Chronic inflammation shifts hematopoiesis toward myeloid lineage expansion while suppressing erythroid differentiation, contributing to anemia and leukocyte imbalance (Liu *et al.*, 2022).

5.5 Mitochondrial Dysfunction in Blood Cells

Many contaminants impair mitochondrial function. Mitochondria regulate:

a. ATP production

b. Apoptosis signaling

c. ROS homeostasis

Heavy metals disrupt mitochondrial membrane potential, leading to:

i. Reduced ATP synthesis

ii. Increased oxidative stress

iii. Activation of apoptotic pathways

In erythrocyte precursors, mitochondrial dysfunction impairs maturation and hemoglobin production. In leukocytes, mitochondrial damage alters immune response efficiency and increases cell death.

5.6 Epigenetic Alterations in Hematopoietic Cells

Emerging evidence suggests that environmental contaminants induce epigenetic modifications affecting gene expression without altering DNA sequence. Observed effects include:

a. DNA methylation changes

b. Histone modification alterations

c. MicroRNA dysregulation

These epigenetic changes influence genes regulating:

i. Hematopoiesis

ii. Immune activation

iii. Tumor suppression

Chronic exposure may therefore reprogram hematopoietic stem cells toward dysfunctional phenotypes.

5.7 Combined Mechanistic Model of Hematotoxicity

Environmental contaminants induce hematotoxicity through an integrated multi-layer mechanism:

Chemical toxicity
↓
Oxidative stress
↓
DNA damage + mitochondrial dysfunction
↓
Microbial dysbiosis and systemic inflammation
↓
Cytokine-mediated marrow suppression
↓
Iron sequestration
↓
Impaired erythropoiesis
↓
Hematological disorders

This cascade explains why exposure often results in multi-factorial blood abnormalities rather than isolated effects, (**Table 4**).

Table 4. Mechanisms of Environmental-Induced Hematotoxicity

Mechanism	Molecular Target	Biological Effect	Hematological Outcome
ALAD inhibition	Heme pathway enzyme	Reduced hemoglobin synthesis	Microcytic anemia
ROS generation	RBC membranes	Lipid peroxidation	Hemolysis
DNA damage	Hematopoietic stem cells	Genomic instability	Leukemia risk
Cytokine activation	Bone marrow niche	Suppressed erythropoiesis	Aplastic anemia
Mitochondrial dysfunction	Cellular ATP production	Apoptosis	Blood cell depletion

6. Microbial Mediation of Hematological Effects

Environmental contaminants reshape microbial ecosystems in soil, water, and the human gut, creating biological conditions that amplify systemic inflammation and hematological dysfunction. Beyond their direct toxic effects, pollutants alter microbial community composition, increase the abundance of opportunistic pathogens, and promote antimicrobial resistance (AMR) gene expansion. These microbial shifts play a central role in mediating the interaction between environmental exposure and blood-related disorders. Recent studies demonstrate that pollutant-induced microbial dysbiosis contributes to chronic immune activation, endotoxin translocation, disrupted iron metabolism, and suppression of hematopoietic stem cell function (Liu *et al.*, 2022; Singh *et al.*, 2023). Therefore, microbial mediation represents a key mechanistic bridge between environmental contamination and hematological abnormalities.

6.1 Lipopolysaccharide (LPS)–Induced Immune Activation

One of the most critical microbial mechanisms linking environmental exposure to blood disorders is lipopolysaccharide (LPS)–mediated immune activation. LPS is a structural component of Gram-negative bacterial cell walls and functions as a potent endotoxin. Polluted environments, particularly contaminated water systems and dysbiotic gut ecosystems, often exhibit increased abundance of Gram-negative bacteria capable of producing LPS. When environmental contaminants compromise intestinal epithelial integrity or when pathogens enter systemic circulation, LPS translocates into the bloodstream. LPS binds to Toll-like receptor 4 (TLR4) on immune cells, activating downstream signaling pathways such as NF-κB and triggering the release of pro-inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α). Persistent activation of these inflammatory pathways suppresses erythropoietin signaling and inhibits erythroid progenitor cell proliferation. Chronic inflammation induced by microbial endotoxins is strongly associated with anemia of inflammation and reduced hemoglobin synthesis (Weiss and Ganz, 2021). Thus, LPS-mediated immune activation provides a direct mechanistic explanation for how microbial dysbiosis translates into measurable hematological impairment.

6.2 Iron Sequestration Through Hepcidin Dysregulation

Iron metabolism is tightly regulated by immune signaling pathways. During microbial infection or systemic inflammation, IL-6 stimulates hepatic production of hepcidin, the master regulator of iron homeostasis. Hepcidin binds to ferroportin, the iron export protein expressed on macrophages, enterocytes, and hepatocytes. This binding leads to ferroportin internalization and degradation, preventing iron from being released into circulation. As a result:

a. Iron becomes trapped inside macrophages

b. Serum iron concentration declines

c. Hemoglobin synthesis is reduced

d. Erythropoiesis is impaired

This inflammatory iron restriction mechanism explains the development of anemia of chronic disease in populations exposed to persistent environmental contamination. Studies demonstrate that elevated hepcidin levels correlate with systemic inflammatory markers and microbial dysbiosis, reinforcing the link between environmental exposure, immune activation, and disrupted hematopoiesis (Alemayehu *et al.*, 2022).

6.3 Microbial Toxins and Direct Bone Marrow Suppression

In addition to endotoxins, certain environmental pathogens produce bioactive toxins that directly affect blood cells and hematopoietic tissue. These toxins include hemolysins, exotoxins, and superantigens. When toxin-producing bacteria enter the bloodstream, particularly following exposure to contaminated water or infected wounds, they can directly damage erythrocytes, induce leukocyte apoptosis, and impair platelet function. Experimental studies indicate that chronic exposure to microbial toxins increases oxidative stress within the bone marrow niche and disrupts hematopoietic stem cell proliferation. This leads to impaired differentiation of erythroid and myeloid cell lineages. Such direct microbial toxicity intensifies hematological damage beyond the inflammatory effects alone, demonstrating that infection and pollution act synergistically in driving blood abnormalities.

6.4 Sepsis-Associated Hematological Dysfunction

Environmental contamination increases human and animal exposure to opportunistic pathogens capable of causing systemic infection. When infection progresses to sepsis, the immune response becomes dysregulated and characterized by excessive cytokine production. Sepsis is strongly associated with multiple hematological complications including:

i. Disseminated intravascular coagulation (DIC)

ii. Platelet consumption

iii. Hemolysis

iv. Bone marrow suppression

v. Leukocyte exhaustion

During sepsis, inflammatory mediators further stimulate hepcidin production, exacerbating iron sequestration and worsening anemia. Because polluted environments increase pathogen load and antimicrobial resistance prevalence, they indirectly heighten the risk of sepsis-related blood abnormalities (Singh *et al.*, 2023).

6.5 Gut–Bone Marrow Axis in Environmental Exposure

Emerging evidence suggests that gut microbiota regulate hematopoiesis through metabolite production and immune signaling. Beneficial microbial metabolites such as short-chain fatty acids (SCFAs), particularly butyrate, support hematopoietic stem cell maintenance and promote immune homeostasis (Ma *et al.*, 2026). However, environmental contaminants reduce the abundance of SCFA-producing bacteria while promoting pathogenic and resistant microbial populations. This shift disrupts metabolic signaling within the gut–immune–bone marrow axis (Rio *et al.*, 2024). Microbial dysbiosis therefore affects:

i. Bone marrow niche stability

ii. Stem cell differentiation balance

iii. Myeloid–erythroid lineage commitment

The concept of a gut–bone marrow regulatory axis highlights how environmental pollution indirectly impairs blood production through microbial-mediated pathways, (**Figure 2**).

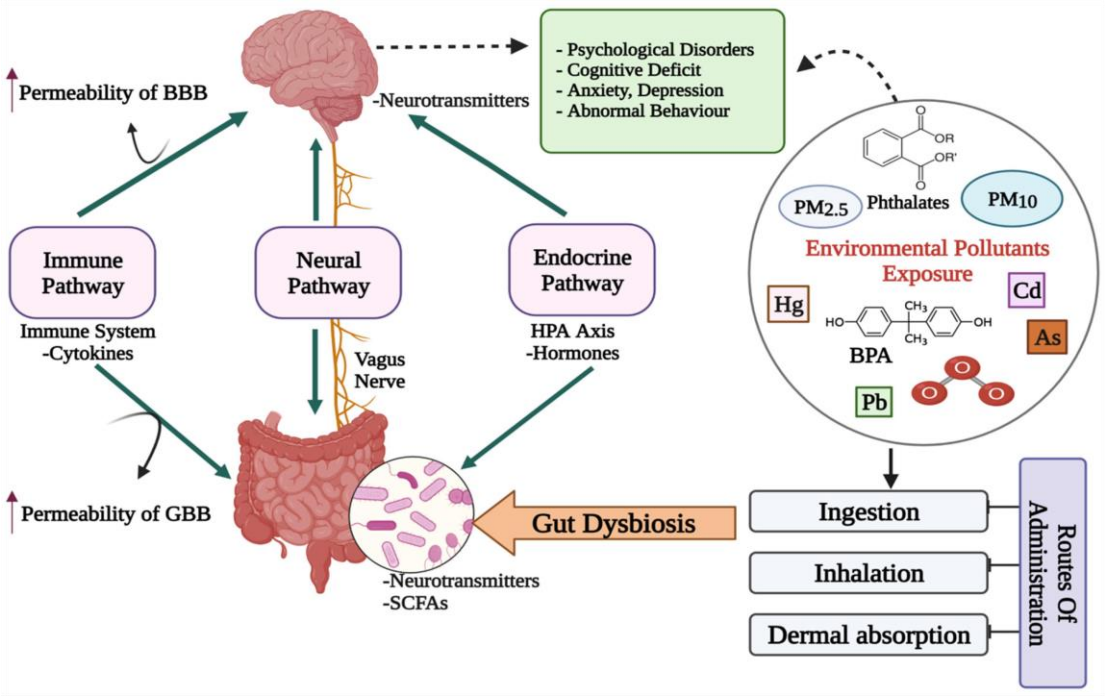

Figure 2. Environmental Polutants on Gut-Bone Marrow Microbiome. https://www.mdpi.com/2076-2607/10/7/1457?utm

6.6 Antimicrobial Resistance and Chronic Infection–Driven Hematotoxicity

Polluted ecosystems act as reservoirs for antimicrobial resistance (AMR) genes and resistant pathogens. Environmental contamination with antibiotics, heavy metals, and industrial waste promotes co-selection of resistance determinants within microbial communities.

When resistant pathogens infect hosts:

i. Treatment duration increases

ii. Pathogen clearance becomes delayed

iii. Infection becomes persistent

Persistent infections maintain prolonged cytokine production, sustained hepcidin elevation, and chronic suppression of hematopoiesis. Therefore, antimicrobial resistance does not only represent a therapeutic challenge, it also functions as an indirect driver of sustained hematological dysfunction by enabling chronic inflammatory stimulation, (**Table 5**). Microbial mediation of hematological effects follows a cascading pathway:

Environmental contamination
↓
Microbial community alteration
↓
AMR expansion + pathogen enrichment
↓
Gut barrier disruption
↓
LPS translocation
↓
TLR4 activation
↓
Cytokine release (IL-6, TNF-α)
↓
Hepcidin upregulation
↓
Iron sequestration + marrow suppression
↓
Anemia and other blood abnormalities

This model demonstrates how microbial ecology functions as a central biological amplifier linking environmental exposure to systemic hematological disease.

Table 5. Microbial Pathways Linking Environmental Exposure to Hematological Dysfunction

Microbial Mechanism	Immune Response	Effect on Iron/Hematopoiesis	Hematological Outcome
LPS translocation	IL-6 activation	Hepcidin upregulation	Anemia
Pathogen invasion	Cytokine storm	Bone marrow suppression	Leukopenia
AMR infection	Chronic inflammation	Persistent iron sequestration	Chronic anemia
Microbial toxin release	Immune activation	Stem cell apoptosis	Blood cell depletion

7. Environmental Contaminants and Specific Blood Diseases

Accumulating epidemiological, experimental, and clinical evidence demonstrates that chronic exposure to environmental contaminants is strongly associated with a broad spectrum of hematological disorders in humans and animals. These disorders arise through interacting mechanisms that include direct cytotoxic injury to blood cells, microbial-mediated systemic

inflammation, disruption of iron metabolism, bone marrow suppression, oxidative stress, and genotoxic damage. Importantly, hematological manifestations often represent early and sensitive indicators of environmental toxicity because blood cells continuously circulate and rapidly respond to systemic inflammatory and chemical insults. Below, we synthesize the evidence linking environmental pollution to specific blood-related diseases and pathological conditions.

7.1 Anemia and Anemia of Chronic Inflammation

Anemia is the most consistently reported hematological abnormality associated with environmental contamination. Heavy metals such as lead (Pb), cadmium (Cd), and arsenic (As) interfere with heme biosynthesis by inhibiting key enzymes such as δ-aminolevulinic acid dehydratase (ALAD). Inhibition of this enzyme reduces hemoglobin synthesis and results in impaired red blood cell production (Jaishankar *et al.*, 2021). Beyond direct enzymatic inhibition, environmental contamination promotes microbial dysbiosis and chronic inflammation. Pollutant-induced activation of immune signaling increases interleukin-6 (IL-6) production, which stimulates hepatic hepcidin synthesis. Elevated hepcidin suppresses ferroportin-mediated iron export from macrophages and intestinal cells, leading to iron sequestration and reduced iron availability for erythropoiesis. This mechanism produces anemia of chronic inflammation, a condition frequently observed in populations living near mining zones, industrial waste sites, and contaminated water sources. Epidemiological studies report significantly lower hemoglobin concentrations and altered red blood cell indices among individuals exposed to high environmental metal burdens compared to control populations (Zhang *et al.*, 2021). In veterinary contexts, livestock consuming contaminated feed and water exhibit reduced packed cell volume (PCV), decreased hemoglobin levels, and impaired oxygen-carrying capacity. Therefore, anemia represents one of the most direct and measurable hematological biomarkers of environmental exposure.

7.2 Leukocyte Abnormalities and Immune Dysregulation

Environmental toxicants significantly alter white blood cell dynamics through multiple pathways. Bone marrow suppression, chronic immune activation, and cytokine imbalance collectively disrupt normal leukocyte production and function. Exposure to benzene, pesticides, heavy metals, and industrial solvents has been associated with:

a. Leukopenia

b. Leukocytosis

c. Altered neutrophil-to-lymphocyte ratio (NLR)

d. Impaired lymphocyte proliferation

e. Dysfunctional macrophage activity

Initially, exposure to microbial endotoxins and inflammatory stimuli may cause leukocytosis as the immune system responds to persistent activation. However, chronic exposure ultimately leads to immune exhaustion and suppression of leukocyte production due to stem cell toxicity and marrow niche disruption. Benzene metabolites are particularly toxic to hematopoietic progenitor cells, leading to decreased lymphoid and myeloid lineage development. Alterations in leukocyte profiles are increasingly recognized as early biomarkers of environmental immune toxicity and systemic inflammatory burden.

7.3 Thrombocytopenia and Coagulation Disorders

Platelets are highly sensitive to oxidative stress and inflammatory mediators generated by environmental exposure. Environmental contaminants induce thrombocytopenia through several mechanisms:

i. Direct toxicity to megakaryocytes in the bone marrow

ii. Suppression of platelet precursor cell differentiation

iii. Immune-mediated platelet destruction

iv. Increased platelet consumption during systemic inflammation

Heavy metals interfere with megakaryocyte maturation, while chronic microbial infections associated with polluted water systems activate coagulation cascades that accelerate platelet consumption. Severe infections arising from environmental exposure can progress to disseminated intravascular coagulation (DIC), characterized by systemic clot formation, platelet depletion, and bleeding complications. DIC represents a life-threatening hematological complication that frequently occurs in septic conditions triggered by environmental pathogens. Thus, pollution-induced infections contribute significantly to coagulopathies and platelet abnormalities.

7.4 Hematological Malignancies (Leukemia and Lymphoma)

One of the most serious long-term consequences of chronic environmental exposure is the increased risk of hematological cancers. Major mechanistic drivers include:

i. Benzene-induced DNA adduct formation

ii. Heavy metal–induced genomic instability

iii. Persistent oxidative stress

iv. Chronic inflammation promoting mutagenesis

Benzene exposure remains one of the strongest established environmental risk factors for acute myeloid leukemia (AML) (Smith *et al.*, 2020). Benzene metabolites accumulate in bone marrow and directly damage hematopoietic stem cells, causing chromosomal aberrations and malignant transformation. Industrial pollutants and contaminated drinking water systems have also been associated with elevated risks of:

a. Non-Hodgkin lymphoma

b. Myelodysplastic syndromes

c. Chronic lymphocytic leukemia

Chronic inflammatory signaling creates a tumor-promoting microenvironment within the bone marrow niche. Continuous cytokine stimulation increases cellular proliferation rates, thereby increasing mutation probability and cancer risk. Environmental carcinogenesis in hematopoietic tissue therefore represents a long-term consequence of combined chemical and microbial stressors.

7.5 Hematological Effects in Animals and Livestock

Environmental pollution impacts not only humans but also livestock, wildlife, and aquatic organisms. Animals exposed to contaminated feed or water demonstrate:

i. Reduced hemoglobin levels

ii. Altered leukocyte counts

iii. Oxidative damage to erythrocyte membranes

iv. Reduced fertility and reproductive capacity

These hematological changes impair oxygen transport, reduce productivity, and increase mortality rates in agricultural systems. Animal models play a crucial role in elucidating mechanistic links between contaminant exposure and blood abnormalities, providing experimental evidence that strengthens causal inference for human health risk assessment. Furthermore, contaminated animal products can serve as secondary exposure pathways for humans, reinforcing the interconnection between environmental and food safety systems.

7.6 Sepsis-Related Hematological Complications

Polluted ecosystems increase exposure to opportunistic pathogens capable of causing systemic infection. When infection progresses to sepsis, profound hematological disturbances occur due to excessive inflammatory activation. Sepsis-associated complications include:

i. Cytokine storm–induced bone marrow suppression

ii. Platelet consumption and thrombocytopenia

iii. Hemolysis

iv. Activation of coagulation pathways

v. Disseminated intravascular coagulation

During sepsis, inflammatory mediators further increase hepcidin production, intensifying iron sequestration and worsening anemia. Because environmental contamination increases pathogen load in water and soil systems, it indirectly elevates the incidence of infection-driven blood abnormalities. Thus, microbial contamination acts as a significant amplifier of hematological risk.

7.7 Dose–Response Relationship and Exposure Duration

Hematological effects of environmental contaminants often follow a dose-dependent and time-dependent pattern. Low-dose chronic exposure typically results in subtle alterations such as:

i. Mild anemia

ii. Slight leukocyte shifts

iii. Early inflammatory marker elevation

Moderate exposure leads to detectable hematological abnormalities including:

i. Significant hemoglobin reduction

ii. Leukocyte imbalance

iii. Platelet dysfunction

High-dose or prolonged exposure may result in:

i. Severe bone marrow suppression

ii. Hematological malignancies

iii. Irreversible blood system damage

Duration of exposure is equally critical. Long-term cumulative exposure increases the probability of permanent genomic damage and malignant transformation. Therefore, both concentration and exposure time determine hematological outcomes.

Table 6. Environmental Exposure and Associated Blood Disorders

Contaminant	Primary Mechanism	Blood Disorder	Evidence Type
Lead	ALAD inhibition, oxidative stress	Microcytic anemia	Epidemiological
Benzene	DNA damage, stem cell toxicity	Leukemia	Occupational studies
Cadmium	Oxidative injury	Anemia	Experimental
Pesticides	Immune suppression	Leukocyte abnormalities	Population studies
Polluted pathogens	Sepsis activation	Coagulopathy	Clinical reports

8. Biomarkers of Environmental Hematotoxicity

Reliable biomarkers are essential for detecting early biological effects of environmental contamination, quantifying exposure burden, and monitoring progression toward hematological dysfunction. Because environmental hematotoxicity operates through multiple interacting mechanisms, including direct toxic injury, oxidative stress, microbial dysbiosis, immune activation, and bone marrow suppression, effective biomarker assessment must integrate chemical, hematological, inflammatory, and molecular indicators (**Table 6**). A multi-parametric biomarker approach provides higher sensitivity and better risk stratification compared to single-marker evaluation (Farahmandian *et al.*, 2025).

8.1 Exposure Biomarkers

Exposure biomarkers quantify the internal dose of environmental contaminants that have entered systemic circulation. These markers directly reflect absorption, bioavailability, and bioaccumulation of pollutants. Commonly measured exposure biomarkers include:

a. Blood lead (Pb) concentration

b. Blood cadmium (Cd) levels

c. Urinary arsenic metabolites

d. Serum mercury levels

e. Detection of pharmaceutical and pesticide residues in blood or urine

Blood-based measurements are particularly important because they represent biologically active toxicant fractions circulating within the hematological system. Biomonitoring studies demonstrate strong correlations between environmental contamination levels and measured blood toxicant concentrations in populations residing near mining zones, industrial regions, and waste disposal sites (UNEP, 2022). These biomarkers provide direct evidence linking environmental pollution to systemic exposure and form the foundation for exposure–response assessment in environmental health research.

8.2 Hematological Biomarkers

Routine hematological indices derived from complete blood count (CBC) analysis remain among the most practical and sensitive indicators of pollution-induced blood abnormalities (Nyarko *et al.*, 2023). Key parameters include:

i. Hemoglobin (Hb) concentration

ii. Red blood cell (RBC) count

iii. Hematocrit (HCT)

iv. Mean corpuscular volume (MCV)

v. White blood cell (WBC) count

vi. Platelet count

Reductions in hemoglobin and RBC indices typically signal impaired erythropoiesis, iron restriction, or toxic suppression of bone marrow function. Alterations in leukocyte and platelet counts reflect immune dysregulation and coagulation disturbances that often accompany chronic inflammatory exposure. Numerous occupational and environmental studies show significant correlations between elevated environmental contaminant levels and abnormal CBC parameters, supporting their utility as early screening tools for hematotoxicity (Pereira *et al.*, 2010). Because CBC testing is inexpensive and widely available, it serves as a primary surveillance instrument in population-level environmental monitoring programs.

8.3 Iron Metabolism and Inflammatory Biomarkers

Microbial-mediated inflammation plays a central role in disrupting iron homeostasis under conditions of environmental exposure. Therefore, biomarkers regulating iron metabolism and inflammatory activation are critical for understanding mechanism-driven hematotoxicity. Important biomarkers include:

a. Hepcidin

b. Ferritin

c. Serum iron

d. Transferrin saturation

e. Total iron-binding capacity (TIBC)

Hepcidin is the master regulator of iron export. Elevated hepcidin levels indicate inflammatory stimulation, typically driven by interleukin-6 (IL-6) produced during microbial dysbiosis or systemic immune activation. When hepcidin increases, ferroportin is degraded, iron becomes trapped within macrophages, and serum iron levels decline. This process results in iron-restricted erythropoiesis and anemia of chronic inflammation. Inflammatory biomarkers that accompany this pathway include:

i. Interleukin-6 (IL-6)

ii. Tumor necrosis factor-α (TNF-α)

iii. C-reactive protein (CRP)

Elevated levels of these cytokines are frequently observed in populations exposed to polluted environments and correlate with both microbial imbalance and hematological suppression (Liu *et al.*, 2022). Thus, combining iron markers with inflammatory markers provides mechanistic insight into pollution-induced anemia.

8.4 Oxidative Stress Biomarkers

Oxidative stress represents a fundamental biological mechanism through which environmental contaminants damage blood cells and hematopoietic tissue (Omar *et al.*, 2022). Heavy metals, pesticides, and industrial chemicals generate reactive oxygen species (ROS), leading to lipid peroxidation, DNA damage, and protein oxidation. Validated oxidative stress biomarkers include:

a. Malondialdehyde (MDA), marker of lipid peroxidation

b. 8-hydroxy-2'-deoxyguanosine (8-OHdG), marker of oxidative DNA damage

c. Reduced glutathione (GSH) levels

d. Superoxide dismutase (SOD) activity

e. Catalase activity

Elevated MDA levels indicate oxidative damage to red blood cell membranes, reducing membrane stability and increasing hemolysis risk. Reduced antioxidant enzyme activity reflects depletion of protective defense systems in response to chronic pollutant exposure. Studies consistently demonstrate increased oxidative stress biomarkers in individuals exposed to heavy metals and industrial emissions, confirming oxidative injury as a central pathway of hematotoxicity. **Figure 3** illustrates the relationship between soil and water polution with Cadiovascular-Oxidative stress biomarkers.

8.5 Microbial Biomarkers

Because microbial dysbiosis mediates hematological dysfunction, microbial indicators are increasingly recognized as critical biomarkers in environmental health research. Relevant microbial biomarkers include:

i. Gut microbiome sequencing profiles

ii. Firmicutes/Bacteroidetes ratio

iii. Relative abundance of pathogenic taxa

iv. Quantification of endotoxin-producing bacteria

v. Detection of antimicrobial resistance (AMR) genes

vi. Plasma endotoxin (LPS) concentration

vii. Metagenomic sequencing enables detection of pollutant-driven shifts in microbial community structure. In polluted ecosystems, increased abundance of AMR genes serves as an indicator of selective pressure imposed by contaminants such as heavy metals and antibiotic residues. Measurement of circulating LPS levels further reflects microbial translocation and systemic inflammatory activation. Microbial biomarkers therefore bridge environmental contamination with immune activation and hematological consequences.

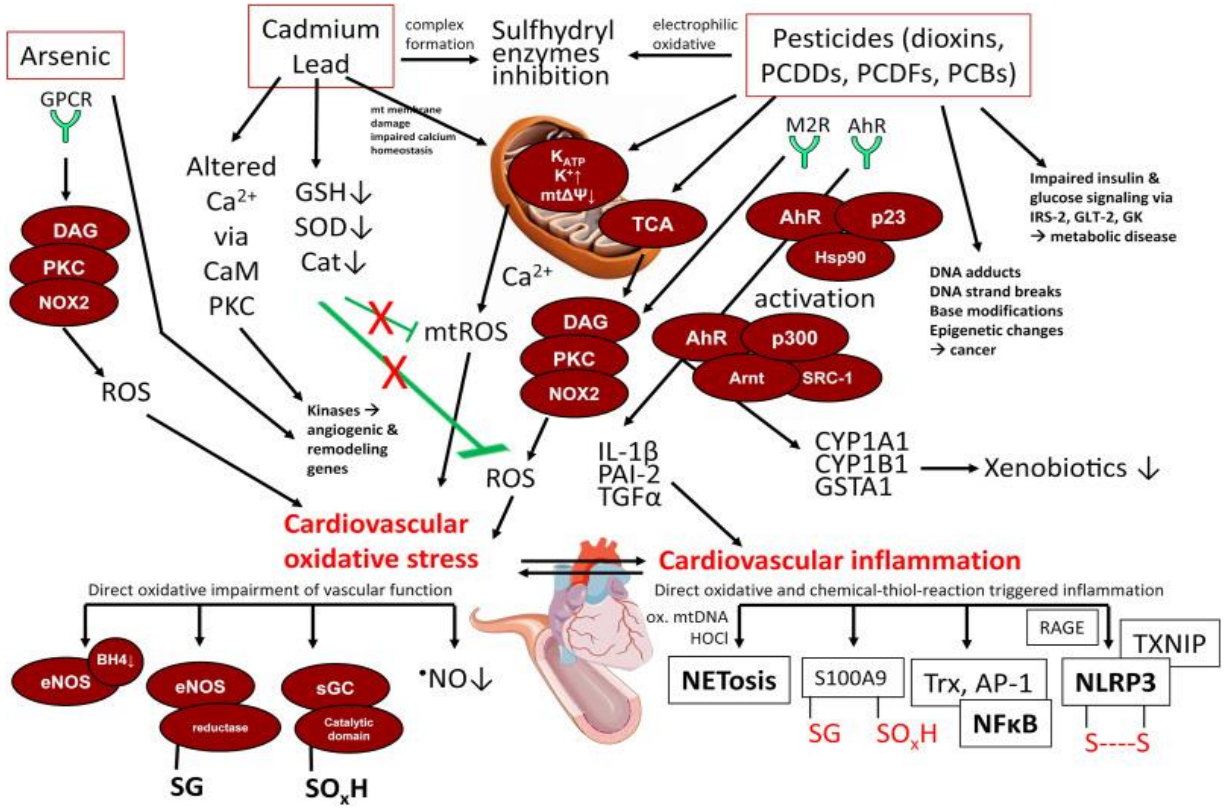

Figure 3. Relationship between water/soil contaminants with cadiovascular-oxidative stress biomarkers. https://www.sciencedirect.com/science/article/pii/S0021915025000577?utm

8.6 Genetic and Epigenetic Biomarkers

Environmental contaminants induce genomic instability and epigenetic modifications that may predispose to hematological malignancies. Key genetic and epigenetic indicators include:

i. Micronucleus assay frequency in peripheral blood lymphocytes

ii. DNA strand break detection

iii. Chromosomal aberration analysis

iv. Global and gene-specific DNA methylation changes

v. MicroRNA (miRNA) expression alterations

The micronucleus assay is widely used to evaluate chromosomal damage caused by genotoxic agents such as benzene and heavy metals. Epigenetic modifications can alter gene expression patterns in hematopoietic stem cells, potentially initiating malignant transformation. These biomarkers provide early warning signals for carcinogenic progression within bone marrow tissue.

8.7 Integrated Biomarker Approach

No single biomarker adequately captures the complexity of environmental hematotoxicity. Therefore, effective monitoring requires integration of:

i. Exposure biomarkers

ii. Hematological indices

iii. Iron metabolism markers

iv. Inflammatory cytokines

v. Oxidative stress indicators

vi. Microbial profiles

vii. Genetic/epigenetic alterations

A multi-layered biomarker strategy improves diagnostic sensitivity, enables mechanistic interpretation, and enhances risk prediction accuracy. Such integrated assessment frameworks are essential for developing evidence-based environmental policies and early intervention strategies, (**Table 7**).

Table 7. Biomarkers for Monitoring Environmental Hematotoxicity

Biomarker Category	Specific Marker	Biological Significance	Application
Exposure	Blood Pb, Cd	Internal toxicant dose	Risk assessment
Hematological	Hemoglobin	Anemia detection	Clinical screening
Iron metabolism	Hepcidin	Inflammation-driven iron sequestration	Mechanistic insight
Oxidative stress	MDA, 8-OHdG	Cellular and DNA damage	Toxicity evaluation
Microbial	Gut sequencing, AMR genes	Dysbiosis detection	Environmental monitoring

9. Risk Assessment and Global Policy Implications

The growing evidence linking environmental contamination to microbial dysbiosis and hematological disorders demands a shift in how environmental risks are assessed and managed. Traditional regulatory approaches primarily evaluate contaminants based on chemical concentration thresholds and direct toxicological endpoints. However, current research demonstrates that pollutants exert systemic biological effects through interconnected pathways involving microbial ecosystem disruption, immune activation, iron metabolism dysregulation, oxidative stress, and bone marrow suppression (Balali-Mood *et al.*, 2022). Risk assessment models must therefore evolve beyond isolated chemical measurements and incorporate biological response indicators that reflect downstream hematological consequences.

9.1 Limitations of Current Risk Assessment Models

Existing environmental regulatory systems rely largely on maximum contaminant levels, permissible exposure limits, and environmental concentration monitoring. Although these parameters remain necessary, they are insufficient for capturing the complexity of real-world exposure scenarios. Environmental samples rarely contain single contaminants. Instead, populations are exposed to complex mixtures of heavy metals, pesticides, pharmaceuticals, microplastics, industrial chemicals, and microbial pollutants simultaneously. These mixtures often produce additive or synergistic effects that amplify systemic inflammation and hematological damage (Gao *et al.*, 2025). Additionally,

chronic low-dose exposure is frequently underestimated. Continuous exposure to pollutant levels below established thresholds can induce cumulative oxidative stress, epigenetic modifications, and gradual bone marrow dysfunction that remain undetected until clinical disease emerges.

Another limitation is the failure to incorporate microbiome-mediated toxicity into regulatory models. Environmental contaminants significantly alter microbial communities in soil, water, livestock, and the human gut. These microbial shifts promote endotoxin release, antimicrobial resistance expansion, and chronic immune activation, all of which contribute to blood abnormalities. Therefore, future risk assessment frameworks must integrate chemical, microbial, and biological indicators into a unified evaluation system.

9.2 Integrating Microbial Indicators into Environmental Risk Models

Because microbial dysbiosis mediates hematological dysfunction, environmental monitoring should include microbiological parameters alongside chemical testing. Enhanced risk models should incorporate:

a. Assessment of microbial diversity indices in contaminated soil and water

b. Quantification of antimicrobial resistance gene abundance

c. Detection of pathogenic bacterial enrichment

d. Measurement of endotoxin (lipopolysaccharide) concentrations

The integration of metagenomic sequencing with chemical contaminant analysis allows for early detection of ecological disturbances that may precede clinical hematological disorders. Microbial surveillance serves as an early-warning system, identifying environmental instability before population-level blood abnormalities become widespread. Such an approach supports predictive environmental health management rather than reactive intervention.

9.3 Biomonitoring and Public Health Surveillance

Effective prevention of pollution-associated hematological disorders requires structured biomonitoring programs at community and national levels. Public health surveillance should evaluate:

a. Blood levels of environmental contaminants

b. Complete blood count parameters

c. Iron metabolism markers

d. Inflammatory cytokine profiles

e. Microbiome composition in high-risk populations

Longitudinal monitoring is essential to track changes in anemia prevalence, leukocyte abnormalities, platelet dysfunction, and early markers of hematological malignancy. High-risk groups include communities located near mining operations, industrial zones, agricultural regions with intensive pesticide use, and areas with inadequate wastewater management. Establishing integrated surveillance systems enables early detection of exposure clusters and supports timely public health interventions before irreversible hematological damage occurs.

9.4 Policy Recommendations

Mitigating environmental hematotoxicity requires coordinated action across environmental, agricultural, medical, and regulatory sectors. Strengthening environmental regulation is critical. Governments must enforce strict control over industrial emissions, hazardous waste disposal, and heavy metal discharge into soil and water systems. Upgrading wastewater treatment infrastructure is essential to reduce chemical pollutants and microbial contamination. Pharmaceutical and antibiotic pollution must also be addressed. Improved waste management systems, responsible drug disposal practices, and advanced wastewater treatment technologies should be implemented to limit pharmaceutical residues in ecosystems. Reducing unnecessary antibiotic use in healthcare and agriculture will also limit antimicrobial resistance expansion, (Belkaid *et al.*, 2013)

Controlling the spread of antimicrobial resistance is another priority. Environmental surveillance programs should monitor resistance gene distribution in water bodies, agricultural soils, and livestock environments. Restricting non-therapeutic antibiotic use will reduce selection pressure for resistant pathogens that contribute to chronic infection and hematological complications. Adopting a One Health framework ensures integrated management of human, animal, and environmental health. Cross-sector collaboration enables monitoring of pathogen transmission, pollution-related blood abnormalities in livestock, and zoonotic infection risks associated with contaminated ecosystems, (McCormack *et al.*, 2022).

9.5 Global Health Implications

Environmental hematotoxicity disproportionately affects low- and middle-income countries where industrial pollution is increasing and regulatory enforcement remains limited.

Populations in these regions often experience:

i. Higher exposure burdens to heavy metals and toxic chemicals

ii. Limited access to routine hematological screening

iii. Delayed diagnosis of pollution-related blood disorders

These disparities contribute to widening global health inequalities.

International cooperation is necessary to strengthen environmental remediation efforts, build laboratory capacity for biomonitoring, and support technological innovation for pollution reduction. Investment in preventive environmental health strategies reduces long-term healthcare costs and improves resilience against pollution-driven hematological diseases.

Such integrated assessment frameworks are essential for developing evidence-based environmental sustainability policies and One Health intervention strategies (Ajekwe *et al.*, 2025).

10. Discussion, Research Gaps and Future Directions

10.1 Overall Discussion

The evidence synthesized in this review demonstrates that environmental contaminants exert hematological effects through interconnected chemical, microbial, immunological, and molecular pathways. Rather than acting solely as direct hematotoxins, pollutants function as systemic biological disruptors that alter microbial ecosystems, activate chronic inflammatory signaling, impair iron metabolism, induce oxidative stress, and suppress hematopoietic stem cell function (Landrigan *et al.*,

2020; WHO, 2022). A key insight emerging from this integration is that microbial dysbiosis represents a central intermediary mechanism linking environmental exposure to blood disorders. Pollutant-induced shifts in soil, water, and gut microbial communities promote the expansion of endotoxin-producing bacteria, antimicrobial resistance genes, and opportunistic pathogens. These microbial alterations trigger lipopolysaccharide-mediated immune activation, elevate pro-inflammatory cytokines such as IL-6 and TNF-α, and stimulate hepcidin-driven iron sequestration. The resulting inflammatory environment disrupts erythropoiesis and contributes to anemia of chronic disease, leukocyte dysfunction, and platelet abnormalities (Weiss and Ganz, 2019; Liu *et al.*, 2022). In parallel, direct chemical toxicity from heavy metals, pesticides, pharmaceuticals, and emerging contaminants induces oxidative damage to red blood cells and hematopoietic progenitors. Genotoxic stress from compounds such as benzene promotes chromosomal instability and increases the risk of hematological malignancies. When combined with chronic microbial-mediated inflammation, these toxic insults create a synergistic environment that amplifies hematopoietic suppression and carcinogenic transformation (Smith *et al.*, 2020; ATSDR, 2021).

Importantly, hematological abnormalities represent measurable and early biomarkers of environmental exposure. Changes in hemoglobin levels, leukocyte counts, iron parameters, inflammatory markers, and oxidative stress indicators provide practical tools for monitoring pollution-associated systemic toxicity. However, current evidence remains fragmented across disciplines, and integrated mechanistic validation is still limited (Kumar *et al.*, 2023). Overall, the findings support a unified environmental–microbial–immune–hematological axis model in which contamination triggers biological cascades that ultimately manifest as blood-related diseases in humans and animals.

10.2 Integrated Discussion of Mechanisms and Evidence

The convergence of toxicological, microbiological, and hematological evidence indicates that environmental exposure should no longer be assessed solely through direct cytotoxic endpoints. Instead, pollution acts as a systemic modifier of host–microbe interactions and immune regulation.

Heavy metals such as lead, cadmium, and arsenic disrupt heme synthesis by inhibiting key enzymatic pathways while simultaneously generating reactive oxygen species that damage erythrocyte membranes. These direct effects are compounded by microbial dysbiosis, which increases endotoxin translocation and sustains inflammatory signaling (Jaishankar *et al.*, 2021; WHO, 2022). Similarly, organic pollutants and pesticides impair immune regulation and alter gut microbial composition. Reduced abundance of beneficial short-chain fatty acid–producing bacteria weakens intestinal barrier integrity and disrupts the gut–bone marrow regulatory axis. This shift reduces hematopoietic stem cell support and promotes inflammatory suppression of erythropoiesis (Belkaid and Hand, 2014; Liang *et al.*, 2020).

Environmental contamination also contributes to antimicrobial resistance expansion. Polluted ecosystems serve as reservoirs for resistance genes that facilitate chronic infections with treatment-resistant pathogens. Persistent infections prolong inflammatory activation, maintain elevated hepcidin levels, and intensify iron sequestration. Consequently, antimicrobial resistance indirectly sustains hematological dysfunction beyond acute infection events (Martínez *et al.*, 2015; Murray *et al.*, 2022).

Another important observation is that sepsis arising from exposure to contaminated water and soil represents a major acute pathway linking environmental pathogens to severe blood abnormalities.

Sepsis triggers systemic coagulation disturbances, platelet depletion, hemolysis, and bone marrow suppression, reinforcing the connection between environmental microbial contamination and hematological collapse (Singer *et al.*, 2016). From a biomarker perspective, integrated monitoring that combines exposure assessment, hematological indices, inflammatory markers, oxidative stress parameters, and microbial profiling provides the most comprehensive evaluation of risk. However, such integrated approaches remain underutilized in both research and regulatory practice. Thus, current evidence strongly supports the concept that environmental hematotoxicity is not a single-mechanism phenomenon but a multi-layered biological process driven by chemical–microbial–immune interactions.

10.3 Research Gaps and Future Directions

Despite advances in understanding environmental contributions to hematological disorders, several critical research gaps remain.

First, most available studies are cross-sectional and associative in nature. Longitudinal cohort studies are required to determine temporal relationships between exposure, microbial alteration, inflammatory activation, and hematological decline. Without time-sequenced data, causality remains partially inferred rather than conclusively demonstrated (Vrijheid *et al.*, 2016).

Second, mechanistic validation at the molecular level remains incomplete. Future research should combine metagenomics, metabolomics, transcriptomics, and single-cell sequencing to identify specific microbial metabolites and signaling pathways that directly regulate hematopoietic stem cell behavior. Multi-omics integration will provide deeper mechanistic insight into the gut–bone marrow and environment–immune axes.

Third, research on emerging contaminants such as nanoplastics, pharmaceutical mixtures, endocrine disruptors, and PFAS in relation to blood disorders is still limited. These pollutants are increasingly detected in environmental systems, yet their cumulative hematological effects remain poorly characterized (Wang *et al.*, 2022).

Fourth, exposure quantification requires improvement. Environmental concentration measurements alone do not accurately represent internal biological dose. Future studies should integrate personal exposure monitoring with biomarker-based internal dose assessment to establish more accurate dose–response relationships.

Fifth, standardized biomarker panels for environmental hematotoxicity need to be developed and validated across diverse populations. Such panels should combine hematological indices, iron metabolism markers, inflammatory cytokines, oxidative stress parameters, and microbial indicators to improve diagnostic precision (Mitra *et al.*, 2022).

Finally, translational research should focus on integrating environmental exposure history into routine clinical evaluation of unexplained anemia, leukopenia, thrombocytopenia, and hematological malignancies. Public health surveillance systems should incorporate environmental monitoring data to enable early identification of pollution-associated blood disease clusters.

Future investigations should also adopt advanced analytical tools such as artificial intelligence–driven risk modeling and spatial exposure mapping to predict high-risk regions and vulnerable populations.

Addressing these research gaps will strengthen causal inference, improve regulatory frameworks, and facilitate the development of preventive strategies to mitigate environmental hematotoxicity.

11. Conclusion

This review demonstrates that environmental contaminants contribute to hematological disorders through complex and interconnected chemical, microbial, immunological, and molecular mechanisms. Rather than acting solely as direct hematotoxins, pollutants function as systemic biological disruptors that alter microbial ecosystems, promote antimicrobial resistance, trigger chronic inflammation, impair iron metabolism, and suppress hematopoietic stem cell function.

Accumulating evidence supports the existence of an environmental–microbial–immune–hematological axis in which contamination-induced microbial dysbiosis facilitates endotoxin translocation and sustained inflammatory signaling. This cascade elevates pro-inflammatory cytokines, stimulates hepcidin-mediated iron sequestration, increases oxidative stress, and ultimately disrupts erythropoiesis, leukocyte balance, and platelet production. In addition, direct genotoxic effects from contaminants such as heavy metals and benzene increase the risk of hematological malignancies.

Importantly, hematological abnormalities serve as early and measurable biomarkers of environmental exposure in both humans and animals. Integrated monitoring strategies that combine chemical exposure assessment, hematological indices, inflammatory markers, oxidative stress parameters, and microbial profiling provide the most comprehensive approach to risk evaluation.

Despite significant advances, current research remains fragmented and largely cross-sectional, limiting causal inference. Future studies should adopt longitudinal designs, multi-omics integration, and advanced exposure modeling to clarify mechanistic pathways and improve predictive accuracy.

From a policy perspective, environmental risk assessment frameworks must evolve to incorporate biological mediators and microbial indicators alongside traditional chemical thresholds. Implementing a One Health approach is essential for mitigating pollution-driven hematotoxicity and protecting ecosystem, animal, and human health.

Overall, addressing environmental contamination is not only an ecological priority but also a critical intervention for preventing systemic blood disorders and reducing global disease burden.

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