Comprehensive Review on the Toxic Effects of Mercury in Infants and Children: The Role of Mercury in Microbial Pathogenesis, Microbiome Shifts, and Microbial Metallomics

This comprehensive review synthesizes current knowledge on mercury's toxic effects in infants and children, with particular emphasis on microbial interactions, microbiome dysbiosis, and the emerging field of microbial metallomics.

Introduction: Mercury as a Global Health Threat to Vulnerable Populations

Mercury remains one of the most toxic and persistent environmental pollutants with profound implications for human health, particularly among vulnerable populations including pregnant women, infants, and children [1]. The global burden of mercury contamination encompasses multiple exposure sources, creating a complex public health challenge that demands comprehensive understanding of the metal's behavior in biological systems and its interactions with microbial communities [2].

Mercury exists in three primary forms—**elemental, inorganic, and organic**—each presenting distinct toxicological profiles with varying bioavailability and potency [3]. Among these forms, methylmercury (MeHg) emerges as the most neurotoxic and bioaccumulative form, representing the greatest concern for pediatric populations [4]. The developing brain is particularly susceptible to mercury toxicity, with critical windows of vulnerability during prenatal and early postnatal periods when rapid neurological development and synaptogenesis occur [5].

Mercury contamination extends beyond direct exposure pathways to encompass indirect effects mediated through alterations in gut microbial communities, which fundamentally influence absorption, metabolism, and toxicity of this metal. Recent evidence highlights an underappreciated dimension of mercury toxicity: its capacity to disrupt gut microbiota composition and function, thereby creating a pathogenic cascade that amplifies mercury's harmful effects through microbial-mediated pathways [6]. The intersection of mercury toxicology with microbial pathogenesis represents a frontier in understanding how environmental toxicants compromise both host immunity and developmental trajectories in children.

Dietary Exposure: Fish and Seafood as Primary Vectors

Fish and seafood consumption represents the predominant pathway for methylmercury exposure in most human populations, with implications particularly severe for pregnant women and their developing offspring [7]. The bioaccumulation and biomagnification of methylmercury through aquatic food webs create elevated concentrations in predatory fish species, exposing consumers to levels capable of inducing neurodevelopmental impairment [4].

Mercury Sources

Mercury enters aquatic ecosystems through both **anthropogenic sources (70%)** and natural sources (30%), subsequently undergoing microbial methylation in sediments and water columns to form the highly toxic methylmercury that accumulates in fish tissues [7].

Population Impact

Epidemiological studies have documented that an estimated **316,588 to 637,233 children** are born annually in the United States with cord blood mercury levels associated with measurable IQ loss [7].

Risk-Benefit Paradox

The protective effects of omega-3 fatty acids in fish create a complex risk-benefit scenario for pregnant women, as fish consumption provides essential docosahexaenoic acid (DHA) critical for fetal brain development, yet simultaneously exposes mothers to methylmercury [8].

Recent experimental evidence demonstrates that maternal DHA supplementation can ameliorate methylmercury-induced neurotoxicity in offspring through upregulation of DHA metabolites including 19,20-dihydroxydocosapentaenoic acid and 19,20-epoxydocosapentaenoic acid, which appear to suppress oxidative stress and support neuronal development [8]. This finding underscores the importance of identifying populations consuming contaminated fish and implementing targeted interventions to optimize both protective and harmful factors.

Household and Occupational Exposures

While dietary sources dominate population-level exposure, household and occupational exposures present acute risks, particularly for children in developing nations and among vulnerable communities [9]. Case reports document children with acrodynia and severe neurotoxic symptoms resulting from exposure to liquid mercury in household products including jewelry cleaners, light bulbs, and mercury-containing lollipops, with serum mercury concentrations reaching **40.9 µg/L** compared to reference values below 5 µg/L [9].

Artisanal Gold Mining

Artisanal and small-scale gold mining represents the largest anthropogenic source of mercury emissions globally, with miners and their families inhaling mercury vapors during amalgamation processes and absorbing mercury through skin during kneading operations—tasks frequently delegated to children [10].

Population surveys of artisanal miners in Brazil revealed increased autoimmune markers (antinuclear autoantibodies and antinucleolar autoantibodies) in workers exposed to inorganic mercury, with three pro-inflammatory cytokines serving as potential biomarkers of mercury-induced immune dysregulation [10].

ARTISANAL GOLD MINING - PLATINUM

Maternal Transfer and Breastfeeding

Lactating women and infants represent a dyadic exposure unit, with breast milk serving as both a beneficial biological fluid and a potential vector for mercury contamination [1]. In study populations from the Gangetic plains of Bihar, India, **74% of lactating women** had breast milk mercury concentrations exceeding the WHO permissible limit (1.7 µg/L), with corresponding 54% of their infants showing mercury concentrations in urine above permissible limits [1].

The close correlation between maternal and infant mercury burden ($r=0.758$, $r=0.539$, $p<0.0001$) reflects placental transfer during pregnancy and subsequent lactational transfer, establishing maternal body burden as a critical determinant of infant exposure [11]. Analysis of breast milk contamination from late lactation period in Ankara, Turkey revealed that mercury was detected in 87% of samples, with elevated mercury levels in breast milk associated with developmental abnormalities in infants assessed with Denver II developmental screening [12].

Placental Transfer

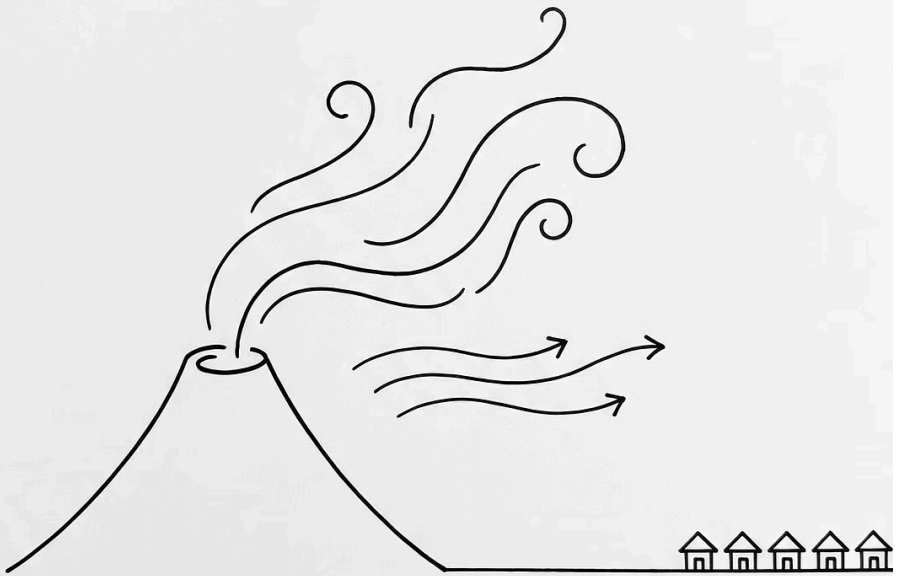
Mercury crosses the placenta during pregnancy

Lactational Transfer

Mercury passes through breast milk to nursing infants

Infant Accumulation

Infants accumulate mercury burden from both pathways



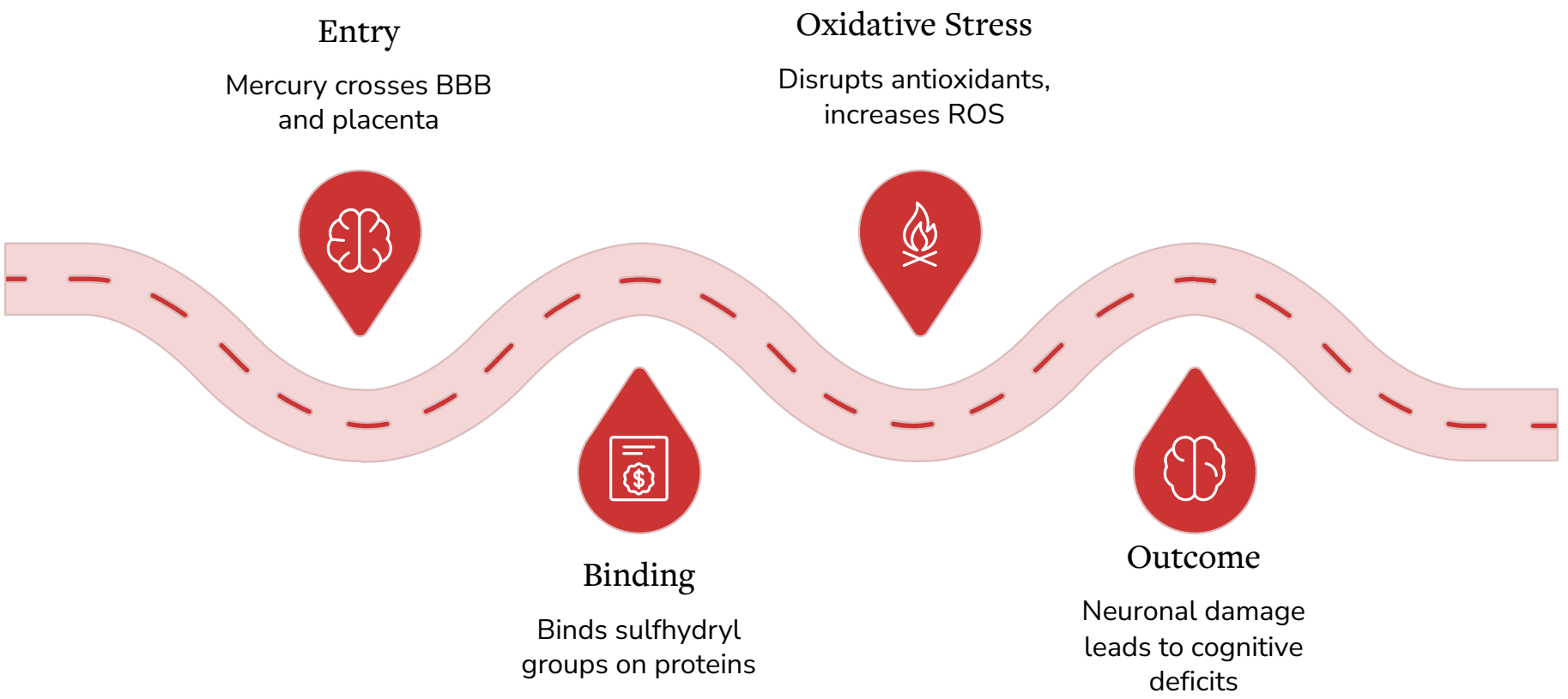
Volcanic and Environmental Mercury Exposure

Populations inhabiting volcanically active regions experience unique exposure scenarios, with gaseous elemental mercury (Hg^0 or GEM) released from geothermal activity creating chronic low-level inhalational exposure [13]. A comparative study of children aged 6-9 years in volcanic versus non-volcanic areas revealed mercury levels in hair of exposed children were **4.2 times higher** than non-exposed controls (1797.84 ± 454.92 ppb vs. 430.69 ± 66.43 ppb, respectively), with preliminary evidence of neurotoxic effects including nervous system damage [13].

This population-based research highlights knowledge gaps regarding the fate, modifications, and health impacts of volcanogenic mercury, particularly regarding long-term effects on developing nervous systems in children chronically exposed to this environmental source.

Neurodevelopmental Impairment and Cognitive Dysfunction

Mercury's capacity to cross the blood-brain barrier and placenta enables direct accumulation in the fetal and developing brain, where it disrupts critical neurodevelopmental processes including synaptogenesis, neuronal migration, and establishment of neural circuits [14]. The Faroe Islands prospective study of methylmercury exposure documented associations between cord blood mercury concentrations and deficits in language, attention, and memory at age 7 years, with greatest susceptibility occurring during late gestation when critical brain development proceeds [15].



Molecular mechanisms underlying mercury neurotoxicity involve covalent binding to sulfhydryl (thiol) groups of proteins, disrupting crucial antioxidant and enzymatic systems including the glutaredoxin/glutathione system, heat-shock chaperones, and glutamate signaling pathways. Mercury-induced oxidative stress in neuronal cells generates reactive oxygen species that damage lipids, proteins, and DNA while simultaneously impairing antioxidant defenses, creating a cascade of cellular injury disproportionately affecting the developing brain [3].

Genetic polymorphisms of catechol-O-methyltransferase (COMT) modify susceptibility to mercury neurotoxicity in children, with boys carrying specific COMT haplotypes showing increased vulnerability to adverse neurobehavioral effects from dental amalgam mercury exposure [16]. This gene-environment interaction underscores the importance of identifying genetically susceptible subpopulations for targeted preventive interventions.

Motor Function, Speech Delays, and Behavioral Alterations

Mercury exposure during critical developmental windows impairs fine and gross motor development, manifesting as delayed motor milestones, reduced grip strength, and impaired motor coordination [8]. Experimental evidence from mercury-exposed mice demonstrates alterations in neurobehavioral function associated with mercury accumulation in brain tissue, increased nitrosative stress (elevated NOx levels), and reduced Na^+/K^+-ATPase activity—an enzyme essential for neuronal excitability and synaptic transmission [17].

Motor Impairment

Delayed motor milestones, reduced grip strength, and impaired motor coordination

Speech and Language Delays

Speech delays, language development disorders, and learning disabilities emerge as measurable outcomes of prenatal mercury exposure

Transgenerational Effects

Perinatal and developmental mercury exposure produces irreversible and severe injuries in offspring, with **F2-generation mice** showing the most significant neurobehavioral dysfunctions, indicating transgenerational neurotoxic effects [17]

In one West Coast health maintenance organization study, delayed speech and language abnormalities correlated with early life mercury exposure, demonstrating that thimerosal-containing vaccines, when combined with dietary methylmercury exposures, may exceed safety thresholds during the critical period of early language acquisition [18]. These neurobehavioral alterations likely reflect disruptions to developing speech and language centers including Broca's and Wernicke's areas, along with disruptions to circuits supporting attention and executive function.

Association with Autism Spectrum Disorder and Developmental Neuropsychiatric Conditions

The association between mercury exposure and autism spectrum disorder (ASD) has emerged as a controversial yet extensively researched area, with multiple lines of evidence suggesting potential causal mechanisms [19]. Meta-analyses examining mercury levels in hair, urine, and blood of children with ASD reveal consistent patterns of elevated mercury compared to typically developing controls, suggesting either heightened exposure or impaired detoxification capacity in ASD populations [20].

Mercury exposure, whether organic or inorganic in form, can produce developmental characteristics and symptoms frequently observed in autism spectrum disorders including **social deficits, communication difficulties, and stereotyped/repetitive behaviors** [19].

Mechanisms of ASD Pathogenesis

The mechanism by which mercury contributes to ASD pathogenesis likely involves disruption of synaptic development and maturation, with particular effects on excitatory-inhibitory balance critical to normal social and communicative development [21].

In vitro studies using human induced pluripotent stem cell (iPSC)-derived neuronal and glial cultures demonstrate that methylmercury, at concentrations mimicking environmental exposure, impairs neurite outgrowth, synaptogenesis, and brain-derived neurotrophic factor (BDNF) expression—key events in early neurodevelopment [21].

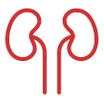
These findings suggest that mercury may act as a developmental neurotoxicant capable of producing autism-like cellular alterations during critical periods of neural circuit formation in susceptible individuals.

Systemic Effects Beyond the Nervous System

While neurotoxicity dominates the literature on mercury's effects in children, evidence increasingly documents toxicity to cardiovascular, renal, immunological, endocrine, and reproductive systems [4]. Mercury exposure has been associated with impaired heart rate variability, particularly following early childhood exposures, suggesting that neurotoxic effects on the autonomic nervous system extend to cardiac autonomic function [22]. In children, chronic mercury exposure may increase oxidative stress through increased production of free radicals, reduction in antioxidant enzyme activity (particularly glutathione peroxidase), and impaired vascular function [22].

Cardiovascular System

Impaired heart rate variability and cardiac autonomic function



Renal System

Glomerulonephritis, tubular dysfunction, and progressive renal failure in severe cases, with developing kidneys potentially more vulnerable to these effects [4]

Immune System

Altered Th1/Th2 balance, suppressed natural killer cell function, and autoimmune responses, and promoting autoimmune responses through molecular mimicry and gap junction disruption [23]

Sleep Regulation

Sleep apnea, excessive daytime sleepiness, and restless leg syndrome from pineal gland accumulation, likely reflecting mercury accumulation in the pineal gland and disruption of circadian rhythms [24]

Mercury-Induced Gut Dysbiosis and Loss of Microbial Diversity

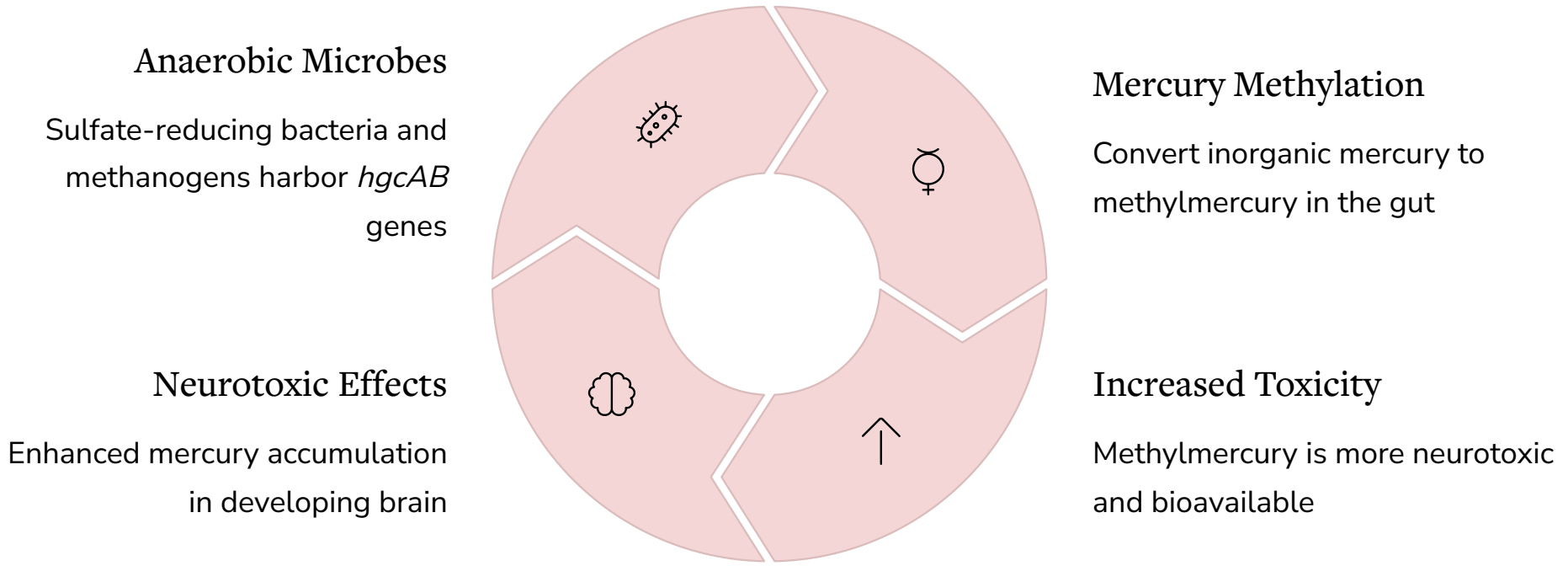
Mercury exposure profoundly disrupts gut microbiota composition through multiple mechanisms, reducing both alpha and beta diversity and shifting the balance toward pathogenic genera [6]. The relationship between heavy metals and gut microbiota is bidirectional: while the gut microbiota can facilitate absorption and metabolism of metals, metals simultaneously alter microbial composition and metabolic function in ways that compromise intestinal barrier integrity and immune homeostasis [6].

Mechanisms of mercury-induced dysbiosis include **oxidative stress to microbial cells, inhibition of essential enzyme systems dependent on metal cofactors, and selective suppression of sensitive commensal taxa while allowing overgrowth of mercury-tolerant pathobionts [25]**.

In animal models of mercury exposure, dysbiosis characterized by reduced commensal bacteria (particularly short-chain fatty acid-producing taxa) and enrichment of potentially pathogenic Proteobacteria emerges as a consistent finding [26]. The loss of beneficial bacteria including *Faecalibacterium*, *Ruminococcus*, *Bifidobacterium*, and other butyrate-producing taxa reduces production of short-chain fatty acids (SCFAs), which critically support intestinal epithelial barrier integrity and regulate immune homeostasis [27]. This depletion of protective microbial metabolites, combined with enrichment of pathogens producing lipopolysaccharides and other pro-inflammatory molecules, creates an intestinal microenvironment conducive to systemic inflammation and immune dysregulation [28].

Methanogens, Sulfate-Reducing Bacteria, and Mercury Methylation by Pathogenic Microbes

Mercury methylation—the conversion of inorganic mercury to neurotoxic methylmercury—occurs primarily through the action of anaerobic microorganisms harboring the *hgcAB* gene pair, a discovery that fundamentally altered understanding of mercury biogeochemistry [29]. Sulfate-reducing bacteria (SRB) represent historically the best-characterized mercury methylators, with metagenomic studies revealing that SRB account for substantial portions of *hgcA* gene transcription in environmental samples despite comprising less than 10% of total *hgcA*-carrying communities [29].



Methanogenic archaea—another major group of methylators—couple mercury methylation to methanogenesis, with the metabolic conditions favoring both processes (anaerobic, sulfate-depleted, organic carbon-rich environments) creating hotspots of methylmercury production [30]. The mechanistic basis of mercury methylation involves *HgcA*, a corrinoid protein, and *HgcB*, a ferredoxin, functioning together in a pathway analogous to tetrahydrofolate-dependent methyl transfer, but utilizing mercury as the substrate [31].

Kinetic studies demonstrate that *HgcAB*-mediated methylation is highly oxygen-sensitive and follows Michaelis-Menten kinetics with apparent Km of **3.2 nM**, indicating remarkable affinity for mercury and capacity to methylate mercury even at extremely low environmental concentrations [31]. Environmental factors including dissolved organic matter, pH, redox potential, and sulfate availability regulate both the abundance of mercury-methylating microbes and their methylation efficiency, suggesting that dysbiosis-driven alterations in the microbial environment could substantially enhance methylmercury production in the intestinal tract [32].

Microbial Metallomics: Assessment of Metal Burdens and Microbe-Metal Interactions

Metallomics—the quantitative analysis of metal element concentrations, speciation, and localization in biological systems—provides critical insights into how infants and children accumulate toxic metals and how microbial communities mediate these processes [11]. Comparative analysis of metal burdens in infant-mother pairs reveals striking patterns: while mercury shows close maternal-infant correlation reflecting placental and lactational transfer, lead, cadmium, and aluminum accumulate to approximately **three-fold higher concentrations** in children compared to their mothers [11].

Differential Metal Accumulation

This differential accumulation suggests that children's developing intestinal barrier and immature detoxification systems may render them more susceptible to metal bioaccumulation than their mothers [11].

Inverse correlations between essential metals (particularly zinc and magnesium) and toxic metals (lead and arsenic, respectively) in pediatric populations suggest that metal competition for absorption and metabolism may amplify toxicity when essential metal status is compromised.

Essential Metal Deficiency

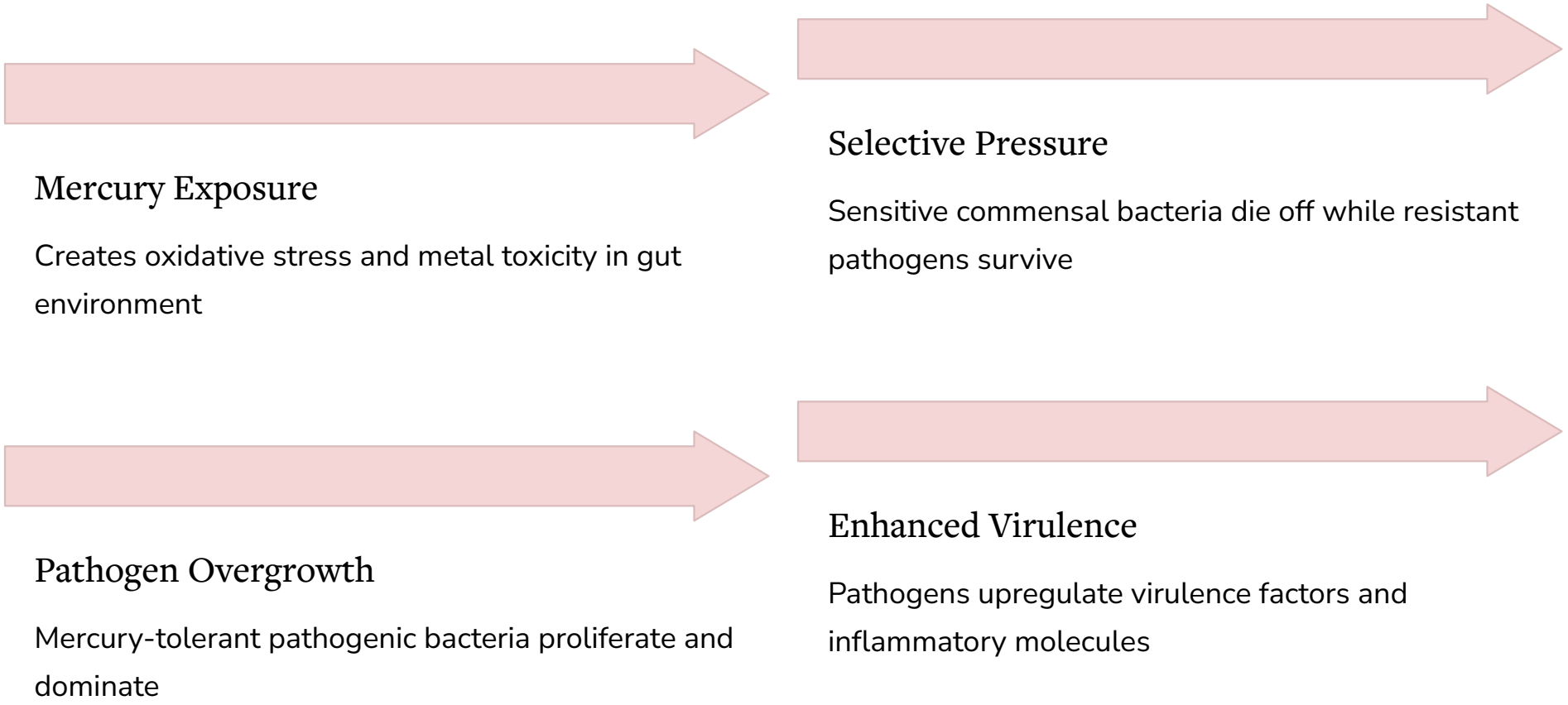
The finding that **37.7% of children** in metalloomic studies showed zinc deficiency, a metal essential for immune function and detoxification enzyme synthesis, suggests a critical vulnerability: the simultaneous assault from toxic metal accumulation combined with essential metal deficiency creates a dual metabolic crisis [11].

Microbial metalloomics has revealed that gut bacteria modulate metal bioavailability through the synthesis of metal-chelating compounds, alterations in pH, and expression of metal-binding proteins, thereby influencing the speciation and bioavailability of both essential and toxic metals [6].

Pathogenic Microbe Overgrowth and Mercury-Mediated Virulence Enhancement

Mercury exposure selectively promotes overgrowth of pathogenic bacteria capable of surviving and proliferating under conditions of oxidative stress and metal toxicity, effectively enriching for virulence traits [6]. Pathobionts including *Desulfovibrio* species, sulfate-reducing bacteria previously considered commensal, demonstrate enhanced pathogenic potential in mercury-exposed microbiota, potentially through upregulation of virulence factors and adhesion molecules [33].

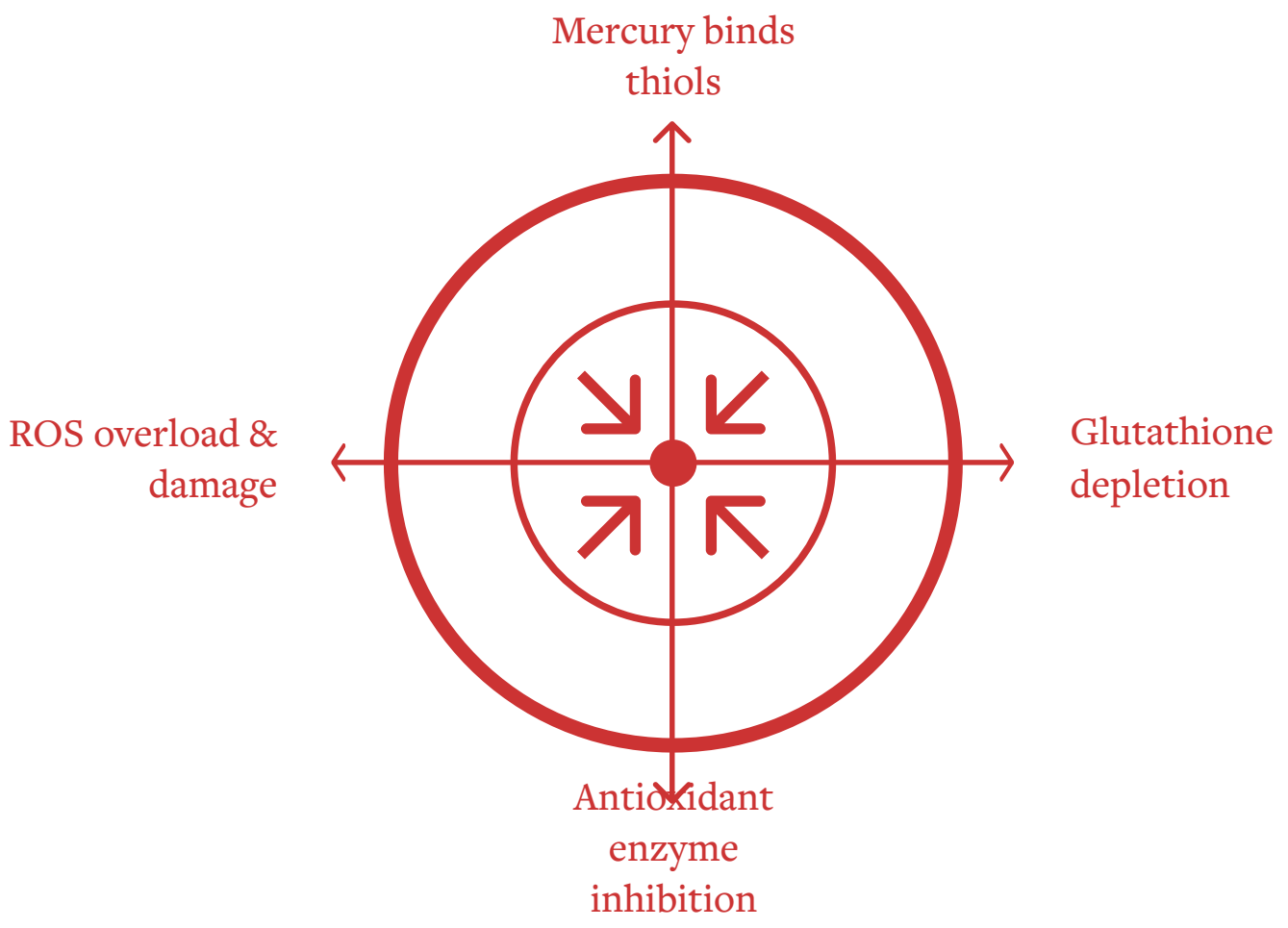
The expansion of Proteobacteria—a gram-negative phylum associated with elevated lipopolysaccharide production—creates a pro-inflammatory microbial community that stimulates toll-like receptor 4 signaling and promotes systemic endotoxemia [27].



The role of mercury in promoting specific pathogenic microbe overgrowth extends to secondary infections and antimicrobial resistance, as dysbiotic communities show reduced capacity to exclude opportunistic pathogens and enhanced susceptibility to bacterial and fungal invasions [34]. In COVID-19 patients, antibiotic-treated dysbiotic microbiota containing blooms of pathogenic bacteria including *Candida* species and antimicrobial-resistant Proteobacteria showed evidence of bacterial translocation into the bloodstream, demonstrating a direct link between dysbiosis severity and life-threatening secondary infections [34]. While direct evidence for similar microbial translocation in mercury-exposed children remains limited, the mechanistic pathways by which dysbiosis promotes bacterial translocation suggest this represents a plausible additional mechanism of mercury pathogenesis.

Oxidative Stress and Antioxidant System Collapse

The generation of excessive reactive oxygen species (ROS) and reactive nitrogen species (RNS) represents a central mechanism by which mercury induces cellular injury across all organ systems [35]. Mercury binds avidly to sulfhydryl groups of glutathione, cysteine, and homocysteine, depleting free thiol pools and inhibiting the synthesis and recycling of the master antioxidant glutathione (GSH), thereby crippling the cell's capacity to neutralize ROS [35].



This glutathione depletion cascades to impair the antioxidant enzyme glutathione peroxidase (GPx), glutathione reductase (GR), and glutaredoxin (Grx)—enzymes entirely dependent on GSH for catalytic function [36]. Additionally, mercury disrupts superoxide dismutase (SOD) and catalase by binding to critical metal cofactors (copper, iron, zinc, magnesium), effectively poisoning these essential antioxidant enzymes at their active sites [35].

In children with autism spectrum disorder, mercury exposure further dysregulates the thioredoxin 1/thioredoxin reductase 1 (Trx1/TrxR1) antioxidant system, a parallel pathway to the glutathione system with critical importance in immune cell function [36]. Methylmercury treatment of neutrophils from ASD children produces **exaggerated ROS accumulation** compared to typically developing controls, suggesting that developmental differences or genetic polymorphisms in children with ASD render their immune cells particularly vulnerable to mercury-induced oxidative stress [36]. This heightened oxidative stress in immune cells of susceptible children likely contributes to immune dysregulation and increased susceptibility to infections or dysbiotic microbial overgrowth.

Immune System Dysregulation, Autoimmune Activation, and Cellular Communication Disruption

Mercury exposure triggers complex alterations in immune regulation, including activation of autoimmune responses and dysregulation of Th1/Th2 balance critical to protection against infections [10]. In artisanal gold miners with occupational mercury exposure, elevated pro-inflammatory cytokines including **TNF-α, IL-1β, and IL-6** associated with detection of antinuclear autoantibodies and antinucleolar autoantibodies, indicating mercury-driven breakdown of immune tolerance [10]. These findings suggest a mechanism by which chronic mercury exposure primes the immune system toward autoimmune activation through molecular mimicry and immune dysregulation.

Innate Immunity

Depression of natural killer cell function and altered macrophage cytokine production

Adaptive Immunity

Reduction in T-lymphocyte proliferation and suppression of antibody responses to infections

Metallothioneins

Metal-binding proteins with immunomodulatory functions are dysregulated by mercury exposure

Mercury impairs both innate and adaptive immune responses through multiple mechanisms: depression of natural killer cell function, reduction in T-lymphocyte proliferation, altered macrophage cytokine production, and suppression of antibody responses to infections [35]. Metallothioneins (MTs), metal-binding proteins with immunomodulatory functions, are dysregulated by mercury exposure in ways that further compromise immune defenses [37]. The modulation of MTs in immune cells regulates metal ion availability, cellular redox status, and cell signaling, with mercury-induced dysregulation creating a cascade of immune dysfunction that extends beyond the direct effects of mercury on immune cells themselves [37].

Gap Junction Dysfunction

Mercury inhibits gap junction-mediated intercellular communication through direct toxic effects on connexin proteins and associated regulatory molecules, effectively isolating cells from tissue-specific homeostatic control [23]. This gap junction disruption in epithelial tissues including the intestine creates "communicational isolation" of cells, potentially promoting their proliferation and loss of normal growth constraints while simultaneously impairing local immune cell signaling [23]. In the context of the intestinal epithelium, mercury-induced gap junction disruption may contribute to increased intestinal permeability ("leaky gut"), allowing translocation of bacterial lipopolysaccharides and pathogenic organisms [23].

The disruption of gap junction communication by mercury has broader implications for developing tissues, as gap junctions mediate critical cell-to-cell signaling during embryonic development and early childhood growth. The period of maximum vulnerability to gap junction-disrupting effects likely coincides with rapid development and tissue remodeling in infancy and early childhood, potentially contributing to developmental delays and structural abnormalities in exposed children [35].

Mitochondrial Dysfunction and Impaired Energy Metabolism

Mercury accumulates in mitochondria and disrupts oxidative phosphorylation through interactions with proteins of the electron transport chain, impairing the cell's capacity to generate ATP [35]. The impairment of mitochondrial respiration by mercury creates an energy crisis in metabolically active cells including neurons, immune cells, and epithelial barrier cells, contributing to reduced function and increased susceptibility to apoptosis [38]. Mercury-induced mitochondrial permeability transition, leading to loss of mitochondrial membrane potential and release of cytochrome c, activates apoptotic cascades in neuronal and immune cells [35].

Vulnerability of the Developing Brain

The developing brain's high metabolic demands and immature antioxidant defenses render it particularly vulnerable to mercury-induced mitochondrial dysfunction [38]. This energy depletion manifests as **impaired synaptic plasticity, reduced synaptogenesis, and deficient long-term potentiation**—mechanisms underlying learning and memory formation [39].

Compounding Metabolic Crisis

The combination of mitochondrial dysfunction in neurons alongside dysbiosis-mediated SCFA depletion (as butyrate serves as a preferred fuel for intestinal epithelial cells and supports the blood-brain barrier) creates a compounding metabolic crisis affecting both the developing brain and the critical intestinal barrier [39].

Biomarker Selection and Assessment Strategies in Mercury-Exposed Children

The selection of appropriate biomarkers for mercury exposure in children requires understanding of mercury's pharmacokinetics, the exposure window of interest, and the biological compartment reflecting that window of exposure [40]. Whole blood mercury concentrations effectively reflect recent dietary methylmercury exposure (2-3 month window) and represent the most commonly used biomarker for population screening [40]. Hair and toenail mercury, reflecting longer exposure windows (months to years), prove valuable for characterizing chronic exposures and identifying vulnerable subpopulations with elevated cumulative mercury burden [40].

01

Blood Mercury

Reflects recent dietary methylmercury exposure (2-3 month window)

02

Hair and Toenail Mercury

Reflects chronic exposure over months to years

03

Metallomics Assessment

Quantifies multiple elements simultaneously to reveal metal-metal interactions

04

Plasma Metal Speciation

Separates metalloproteins from labile metal pools for mechanistic insights

The metallomics approach, quantifying multiple elements simultaneously in pediatric cohorts, reveals critical patterns of metal-metal interactions and differential accumulation patterns between mothers and children [11]. Metallomics assessment of mercury alongside essential metals including zinc, magnesium, iron, and selenium enables identification of dual-metal crises (toxic metal accumulation + essential metal deficiency) requiring integrated intervention strategies [11]. Plasma metal speciation analysis, separating metalloproteins from labile metal pools, provides mechanistic insights into how mercury disrupts protein-bound metal homeostasis, offering potential for identifying functional biomarkers of mercury toxicity beyond simple metal quantification [41].

Prenatal Screening and Risk Stratification

Prenatal assessment of maternal mercury burden through blood testing enables identification of pregnancies at risk for fetal neurotoxic exposure, facilitating timely interventions. The EPA established a reference dose (RfD) of **0.1 µg/kg body weight/day** for methylmercury based on data from the Iraqi methylmercury poisoning epidemic, though subsequent research suggests this dose may be insufficiently protective for vulnerable windows of fetal development. Cord blood mercury measurement at delivery provides objective documentation of fetal exposure and enables correlation with perinatal outcomes, identifying newborns requiring close neurodevelopmental monitoring.

Genetic polymorphisms affecting metal metabolism—including COMT, glutathione S-transferase (GST), and metallothionemercuyn gene variants—show promise as biomarkers identifying genetically susceptible subpopulations warranting enhanced protective measures. A precision medicine approach incorporating genetic screening, metallomics assessment, and environmental exposure assessment could enable targeted interventions for high-risk children, though implementation of such approaches remains limited to research settings and specialized medical centers.

Microbiome Assessment and Clinical Interventions

The characterization of dysbiotic patterns through 16S rRNA gene sequencing and metagenomic analysis offers novel biomarkers of mercury-induced systemic pathology, with microbiota composition potentially reflecting individual mercury burden and susceptibility to toxic effects [26]. The presence of specific pathogenic taxa including enriched *Proteobacteria*, *Desulfovibrio* species, and depleted short-chain fatty acid-producing genera (*Faecalibacterium*, *Ruminococcus*, *Bifidobacterium*) correlates with mercury exposure severity and predicts subsequent inflammatory and neurodevelopmental complications [28].

Metagenomic screening for the presence and expression of *hgcAB* genes—the mercury methylation gene pair—in fecal samples could identify children with dysbiotic communities actively methylating intestinal inorganic mercury to neurotoxic methylmercury, creating an endogenous source of toxicant production [43]. The quantification of bacterial metabolites including short-chain fatty acids, secondary bile acids, and other microbial products provides functional biomarkers of dysbiosis severity and restoration of beneficial microbial function during recovery [44]. Children showing markers of severe dysbiosis combined with elevated mercury burden would benefit from microbiome-targeted interventions including prebiotics, probiotics, and dietary modification to restore protective microbial taxa and reduce endogenous methylmercury production.

Chelation Therapy

Dimercaprol (BAL), DMSA, and DMPS bind mercury and facilitate urinary excretion in acute poisoning cases

Microbiome Restoration

Prebiotics and probiotics restore butyrate-producing bacteria and reduce pathogenic taxa

Dietary Interventions

Foods rich in zinc, selenium, magnesium, and antioxidants support defense capacity and microbial restoration

Exposure Elimination

Dietary modification, household remediation, and occupational protections prevent further contamination

Chelation therapy remains the primary medical intervention for acute mercury poisoning, utilizing agents including dimercaprol (BAL), 2,3-dimercaptosuccinic acid (DMSA), and 2,3-dimercapto-1-propane sulfonic acid (DMPS) to bind mercury and facilitate urinary excretion [35]. However, clinical experience demonstrates that chelation therapy alone proves insufficient for children with chronic low-level exposures and secondary complications of dysbiosis and immune dysfunction. Complementary microbiome-restoration strategies including administration of prebiotics or probiotics showing evidence of restoring butyrate-producing bacteria and reducing pathogenic taxa should be considered as adjunctive therapies [45].

Dietary interventions emphasizing foods rich in essential minerals (zinc, selenium, magnesium) and antioxidant compounds (polyphenols, glutathione-containing foods) support both antioxidant defense capacity and microbial restoration [46]. The elimination of further mercury exposure sources—through dietary modification reducing fish consumption in high-exposure populations, remediation of household mercury sources, and occupational protections for at-risk families—represents the essential foundation upon which medical and dietary interventions build. Future therapeutic approaches incorporating understanding of mercury's microbial interactions may leverage engineered probiotics expressing mercury demethylation genes or mercury-binding microbial compounds to reduce intestinal methylmercury bioavailability and support microbial restoration.

Conclusion: An Integrated Understanding of Mercury Toxicity in Children

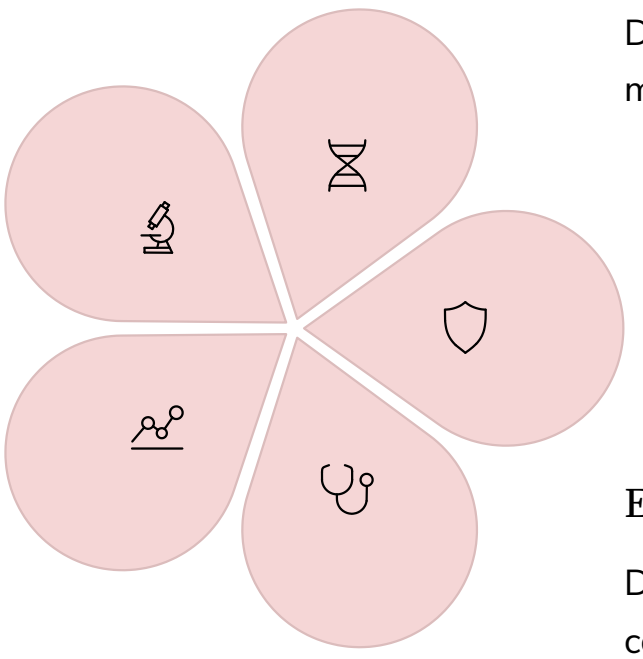
Mercury represents a persistent and multifaceted threat to the health of developing children, operating through direct toxicological effects on the nervous system, immune system, and antioxidant defenses while simultaneously disrupting the critical gut microbiota that mediates both nutrient absorption and immune homeostasis. The emerging recognition of mercury as a driver of dysbiosis—and dysbiosis as a mechanism amplifying mercury's toxic effects through endogenous methylmercury production and barrier dysfunction—fundamentally expands understanding of mercury pathogenesis beyond traditional neurotoxicology.

Microbial Metallomics

Novel biomarkers revealing differential metal accumulation in children

Integrated Research

Combining genomics, metallomics, immunology, and neurodevelopmental assessment



Metagenomic Identification

Detection of mercury-methylating microbes and dysbiotic patterns

Prevention Strategies

Reduction of mercury sources and identification of vulnerable populations

Early Recognition

Detection of dysbiosis-driven complications before severe outcomes

Microbial metalomics approaches revealing differential accumulation of toxic and essential metals in pediatric populations, combined with metagenomic identification of mercury-methylating microbes and dysbiotic patterns, provide novel biomarkers and intervention targets for reducing mercury's burden on developing children. Prevention through reduction of mercury sources, identification of vulnerable populations, and early recognition of dysbiosis-driven complications offers the most promising strategy for protecting children's health in mercury-contaminated environments.

> **Future research integrating microbial genomics, metalomics, immunology, and neurodevelopmental assessment will delineate the mechanisms linking mercury exposure, dysbiosis, and developmental outcomes, enabling development of precision medicine approaches for identification and intervention in affected children.**

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