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Redox-active metals in environmental oxidative stress and disease

Busurat Adenike Mudashiru [1, *], Roqeebat Abiodun Mudashiru [2], Ernest Erenven Isemede [3] and Raphael Okhiria Idewele [4]

[1] *Department of Chemistry, Ohio University, Athens, USA.*
[2] *Department of Chemistry, University of Ilorin, Ilorin, Nigeria.*
[3] *Department of Environmental Health and Technology, University of Eastern Finland, Finland.*
[4] *Department of Wood Materials Science, University of Eastern Finland, Joensuu, Finland.*

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Abstract

Redox-active metals are central drivers of environmentally induced oxidative stress because they can cycle between oxidation states, catalyze reactive oxygen species (ROS) formation, and disrupt endogenous redox signaling. Unlike many organic toxicants that require metabolic activation, metals such as iron, copper, chromium, vanadium, manganese, cobalt, and nickel can directly participate in electron transfer reactions at biological interfaces, including the lung epithelial lining fluid, mitochondrial membranes, lysosomes, and inflamed tissues. Environmental exposure occurs through inhalation of metal-bearing particulate matter, ingestion via contaminated water and food, and dermal contact in occupational and community settings. Once internalized, these metals amplify oxidative burden through Fenton and Fenton-like chemistry, redox cycling, depletion of glutathione and thiol buffers, mitochondrial electron transport chain disruption, and induction of inflammatory NADPH oxidases. Oxidative injury propagates beyond macromolecular damage to include dysregulated redox signaling, epigenetic remodeling, altered proteostasis, and immune activation, creating a mechanistic bridge from exposure to chronic disease. Epidemiologic and toxicologic evidence links metal-rich air pollution and metal exposures to cardiometabolic disorders, neurodegenerative processes, chronic respiratory disease, kidney injury, and carcinogenesis, with susceptibility shaped by genetics, nutrition (iron status), co-exposures (ozone, PAHs, endotoxin), and life stage. This review synthesizes core mechanistic chemistry, biological targets, and disease-relevant pathways, then evaluates biomarker strategies (exposure, effect, and susceptibility) and discusses methodological advances that improve causal inference, including metal speciation, single-cell approaches, and exposome analytics. Finally, it highlights intervention opportunities spanning emission control, exposure reduction, nutritional modulation, and targeted therapeutics that restore redox homeostasis without suppressing physiologic ROS signaling.

Keywords: Redox-active metals; Oxidative stress; Reactive Oxygen Species; Fenton chemistry; Particulate matter; Mitochondrial dysfunction; Inflammation; Epigenetics; Biomarkers; Cardiometabolic disease; Neurotoxicity; Respiratory disease; Carcinogenesis; Metal speciation

1. Introduction: Why metals are uniquely positioned to drive oxidative disease

Oxidative stress is often described as an imbalance between oxidant production and antioxidant defenses, but in biology it is more precise to view it as a disturbance of redox signaling and control [1, 2]. Cells use ROS and reactive nitrogen species (RNS) as regulated messengers to control immunity, vascular tone, and transcription [3, 4]. Environmental exposures become pathogenic when they shift the intensity, location, and timing of oxidant generation beyond what cellular systems can buffer while preserving signaling fidelity. Redox-active metals are unusually potent in this regard because they can generate oxidants catalytically, not stoichiometrically [5, 6]. A small amount of a metal capable of

* Corresponding author: Busurat Adenike Mudashiru.

cycling between oxidation states can repeatedly convert relatively mild oxidants (hydrogen peroxide, organic peroxides) into highly reactive radicals that attack DNA, proteins, and lipids, especially at biological "hot spots" such as membranes and sites of inflammation [7, 8].

The term "redox-active metal" in environmental health typically includes iron (Fe), copper (Cu), manganese (Mn), chromium (Cr), vanadium (V), cobalt (Co), and nickel (Ni), although their biological redox behaviors differ [9]. Some, like Fe and Cu, are essential metals tightly regulated by transporters and storage proteins, yet harmful when in labile pools that catalyze radical formation. Others, like hexavalent chromium (Cr(VI)) and vanadium (V(V)/V(IV)), are not required for human biology but can undergo intracellular reduction steps that generate ROS and DNA-reactive intermediates [10, 11]. Manganese is essential yet neurotoxic at high exposure, in part through oxidative and mitochondrial pathways [12]. Cobalt and nickel have complex redox and hypoxia-mimetic effects, with oxidative stress intersecting with HIF signaling, inflammation, and carcinogenic pathways [13].

Environmental oxidative stress from metals rarely occurs in isolation. Metals co-occur with ultrafine particles, organic combustion products, and secondary oxidants (ozone, nitrogen dioxide), producing mixture effects [14]. Still, metals are frequently among the strongest predictors of the intrinsic oxidative potential of airborne particulate matter, a property measured by acellular assays such as dithiothreitol (DTT) consumption or ascorbate depletion [15]. Understanding how metal chemistry translates into disease therefore requires bridging four layers such as environmental speciation and bioavailability, biological compartmentalization and metal trafficking, enzymatic and non-enzymatic ROS generation, and downstream molecular responses that become chronic pathology.

2. Environmental sources and exposure pathways

Active metals undergo redox reaction and these reactions affect the environment and biological systems as illustrated in Table 1 below. Ambient air pollution is a dominant exposure route for many redox-active metals because combustion and friction processes generate metal-rich particles that deposit efficiently in the respiratory tract [16]. Brake and tire wear contribute Cu, Fe, and other metals; road dust resuspension carries Fe, Mn, and Cr; industrial emissions add Ni, V, Cr, and Co; and oil combustion often contributes Ni and V in characteristic ratios [17]. Wildfires and biomass burning can mobilize metals from vegetation and soils, delivering them in complex matrices with organic carbon and soot that can modify metal solubility and redox behavior [18-20]. Particle size matters such as coarse particles (PM10–2.5) often carry crustal metals and mechanically generated wear debris, while fine (PM2.5) and ultrafine particles more readily reach alveoli and may translocate or influence systemic pathways via inflammation and mediators [21, 22]. Solubility is equally important, a small fraction of soluble or "bioaccessible" metal can dominate acute oxidative effects, because ionic metal species interact readily with epithelial lining fluid, thiols, and redox-active biomolecules [23]. Drinking water can contribute redox-active metals through natural geochemistry (iron- or manganese-rich aquifers), corrosion of distribution systems (iron from pipes), and industrial contamination (chromium, nickel) [24, 25]. Food becomes a pathway through soil-to-plant transfer and through processing and packaging in some contexts. For essential metals, nutritional intake is necessary; the toxicological issue arises when intake is excessive or when metals are present in reactive forms that bypass regulation [26, 27]. Occupational exposures often produce higher and more sustained doses than ambient environments. Welding fumes deliver Fe, Mn, and other metals in ultrafine, highly reactive particles [28]. Metal plating and pigment industries can expose workers to Cr(VI). Oil refining and heavy fuel combustion can yield Ni and V [29, 30]. These settings have helped establish causal links because exposure characterization can be more precise and disease outcomes more clearly associated with metal burdens.

Table 1 Redox-active metals: environmental sources, dominant redox behaviors, and key biological targets

Metal	Common environmental sources	Key redox behavior	Major oxidative mechanisms	Prominent target systems
Iron (Fe)	Road dust, steel industry, welding fumes, soil particles	Fe(II)/Fe(III) cycling	Fenton chemistry, lipid peroxidation, ferroptosis, mitochondrial injury	Lung, cardiovascular system, liver, systemic inflammation
Copper (Cu)	Brake wear, industrial emissions, some water systems	Cu(I)/Cu(II) cycling	Fenton-like reactions, thiol oxidation, protein binding	Lung lining fluid, cardiovascular, oxidative signaling disruption

Manganese (Mn)	Welding, mining, industrial emissions, soil dust	Multiple oxidation states; complex enzymatic roles	Mitochondrial dysfunction, oxidative stress, neuroinflammation	Brain (basal ganglia), lung
Chromium (Cr)	Industrial contamination, plating, pigments, some water sources	Cr(VI) uptake and intracellular reduction to Cr(III)	ROS during reduction, DNA adducts/crosslinks, oxidative damage	Cancer risk, lung, kidney
Vanadium (V)	Oil combustion, industrial emissions, some dusts	V(V)/V(IV) cycling	Redox cycling, phosphatase inhibition, ROS production	Lung, metabolic pathways, inflammation
Nickel (Ni)	Oil combustion, metallurgy, industrial emissions	Variable; often indirect redox effects	Inflammation, oxidative stress, hypoxia signaling perturbation	Respiratory system, carcinogenic pathways
Cobalt (Co)	Metal industry, pigments, some occupational exposures	Redox activity; hypoxia-mimetic effects	Oxidative stress plus HIF stabilization interactions	Lung, systemic inflammation, possible cardiometabolic effects

2.1. Core chemistry of metal-driven oxidative stress

Fenton chemistry is a foundational mechanism as Fe(II) reacts with hydrogen peroxide (H_2O_2) to generate hydroxyl radical (•OH) and Fe(III) [31]. Hydroxyl radical is exceptionally reactive, causing near diffusion-limited attacks on nearby macromolecules. Fe(III) can be reduced back to Fe(II) by superoxide (O_2•−), ascorbate, or cellular reductants, creating a catalytic cycle. Copper can perform analogous reactions through Cu(I)/Cu(II) cycling, and some other transition metals can participate in Fenton-like processes depending on ligand environment [32]. A key toxicological insight is that *location* governs damage. Hydroxyl radical reacts where it is formed, so damage reflects the microenvironment: at membranes it drives lipid peroxidation; near DNA it yields strand breaks and oxidized bases; in proteins it oxidizes side chains and disrupts metal-binding motifs [33, 34]. Thus, "labile" or loosely chelated metal pools in lysosomes, mitochondria, and inflamed extracellular spaces can be more damaging than total metal concentration [35].

Some metals promote oxidative stress by catalyzing redox cycling in the presence of endogenous reductants. Vanadium can cycle between V(V) and V(IV) states, interacting with cellular thiols and producing ROS [36]. Chromium is distinctive: Cr(VI) is taken up by cells via anion transporters (because it resembles sulfate or phosphate), then reduced through intermediate states (Cr(V), Cr(IV)) to Cr(III) [37]. These reduction steps can generate ROS and create DNA adducts and crosslinks via Cr(III) binding. Nickel and cobalt can participate in redox reactions under certain conditions and also influence oxidative balance indirectly through inflammation and hypoxia signaling [38, 39]. Many redox effects are amplified by thiol depletion. Glutathione (GSH) is the dominant cytosolic redox buffer, and protein cysteine residues regulate signaling [40]. Metals can bind thiols, oxidize them, or drive disulfide formation indirectly through ROS. Loss of GSH shifts redox potential and impairs detoxification pathways, including glutathione peroxidase activity and conjugation of electrophiles [41]. In extracellular lung lining fluid, antioxidants such as ascorbate and urate are major defenders; metal-catalyzed depletion of ascorbate is a recognized feature of particle oxidative potential [42]. Iron is essential for oxygen transport and mitochondrial function, but its "labile" pool is dangerous because it supports radical generation. Environmental exposures and inflammation can increase labile iron by damaging ferritin, altering hepcidin signaling, or inducing hemolysis and release of heme iron [43]. Once free iron rises, lipid peroxidation can accelerate and promote a form of cell death called ferroptosis, characterized by iron-dependent accumulation of lipid hydroperoxides [44]. Ferroptosis is increasingly recognized in organ injury and chronic disease contexts, linking metal exposure to tissue remodeling and degeneration [45].

3. Biological targets and pathway architecture

3.1. The lung: first-contact chemistry and immune amplification

The respiratory tract is often the first biological interface for particle-bound metals. Upon deposition, particles encounter epithelial lining fluid rich in antioxidants and proteins. Soluble metals can leach from particle surfaces, and particle-associated redox cycling can proceed at the interface [46]. Oxidative signals activate epithelial stress pathways (MAPK, NF-κB) and induce cytokines (IL-6, IL-8), recruiting neutrophils and macrophages [47]. These immune cells

generate ROS enzymatically via NADPH oxidase and myeloperoxidase, creating a feed-forward loop where metals initiate oxidative stress and inflammation amplifies it. Macrophages can also internalize particles into phagolysosomes where acidic conditions increase metal solubility. Lysosomal membrane permeabilization can release iron and other metals, increasing cytosolic labile pools and promoting mitochondrial injury. Over time, repeated exposure can contribute to airway remodeling, mucus hypersecretion, and altered host defense, increasing vulnerability to infections and exacerbations of chronic respiratory diseases.

3.2. Mitochondria: where metal stress meets energy failure

Mitochondria are both sources and targets of ROS. Many metals impair electron transport chain function, increasing electron leakage and superoxide generation. Mitochondrial DNA (mtDNA) is particularly vulnerable because it lacks protective histones and resides close to the inner membrane where ROS are produced [48]. Oxidative mtDNA damage can trigger innate immune responses through release of mtDNA into the cytosol, activating cGAS-STING pathways and sustaining inflammation [49]. Metals may also disrupt mitochondrial dynamics (fission/fusion), calcium handling, and membrane potential, shifting tissues toward energetic insufficiency, insulin resistance, or cell death pathways [50].

3.3. Endothelium and cardiovascular effects

Cardiovascular disease links to metal-driven oxidative stress through endothelial dysfunction, autonomic imbalance, inflammation, and pro-thrombotic changes. Oxidants reduce nitric oxide bioavailability by reacting with NO to form peroxynitrite, impairing vasodilation [51]. Endothelial cells exposed to metal-rich particles show increased adhesion molecule expression, promoting leukocyte recruitment and vascular inflammation [52]. Oxidative modification of lipoproteins and activation of platelets can contribute to atherogenesis and acute events. Importantly, many studies suggest that the metal component of PM may be particularly associated with cardiovascular risk, consistent with mechanistic plausibility because vascular signaling is exquisitely redox sensitive [53-56].

3.4. Brain and neurodegeneration-relevant pathways

The nervous system is vulnerable because neurons rely heavily on mitochondrial energy and have limited antioxidant reserves in some compartments. Metal exposures can influence neuroinflammation via microglial activation, oxidative injury to dopaminergic circuits (notably with manganese), and disruptions of metal transport and storage [57-59]. Oxidative stress also affects protein folding and aggregation; lipid peroxidation products can modify proteins, potentially contributing to proteostasis collapse seen in neurodegenerative diseases. For essential metals, the boundary between homeostasis and toxicity is narrow, and genetic or nutritional factors that alter metal handling can shape susceptibility [60].

3.5. Kidney and liver: filtering and biotransformation hubs

Kidney injury can reflect both direct metal toxicity and systemic oxidative stress [61]. Metals can accumulate in proximal tubules, where oxidative damage impairs transport functions and promotes inflammation and fibrosis [61]. The liver, as a central organ of metal storage and detoxification, can also experience oxidative injury, particularly when metal exposures interact with metabolic stress (high-fat diet, alcohol) to intensify lipid peroxidation and inflammatory signaling [62].

3.6. Iron and copper: essential metals with toxic labile pools

For Fe and Cu, toxicity often arises when regulatory systems are bypassed. Most iron is bound to hemoglobin, ferritin, or transferrin; most copper is chaperoned by proteins to prevent free Cu catalysis. Environmental particles can deliver soluble forms, while inflammation and oxidative conditions can release iron from ferritin or heme proteins. A major conceptual shift in recent years is that oxidative injury is not only about “more ROS,” but also about a changed metal landscape: increased labile iron drives lipid peroxidation and ferroptosis-like processes, and copper can catalyze extracellular oxidation in lung lining fluid, impairing barrier function and host defense.

4. Oxidative stress as a systems problem: inflammation, epigenetics, and cell death

Environmental metal exposure often triggers inflammation that becomes a major ROS source. Neutrophils generate superoxide; myeloperoxidase produces hypochlorous acid; macrophages produce nitric oxide that reacts with superoxide to form peroxynitrite [63]. Metals can prime these responses, leading to chronic low-grade oxidative burden. This matters because chronic disease is not driven only by acute oxidative damage but by sustained inflammatory-redox remodeling of tissues. Redox changes influence transcription factors such as NF-κB, Nrf2, and AP-1. Nrf2 is a protective pathway: when activated, it induces antioxidant enzymes and detoxification proteins [64, 65]. Some metal exposures

activate Nrf2 adaptively, but repeated exposures may overwhelm this system or lead to maladaptive activation patterns. Metals can also affect DNA methylation and histone modifications indirectly through oxidative stress and directly by disrupting enzymes that require metal cofactors or redox conditions [66, 67]. These epigenetic changes can "store" exposure effects, altering gene expression long after exposure decreases. Cell death pathways are increasingly important for connecting oxidative stress to tissue remodeling. Ferroptosis, driven by iron-dependent lipid peroxidation and failure of GPX4-mediated lipid peroxide detoxification, is a compelling mechanism in lung injury, kidney injury, and possibly neurodegeneration [68-70]. Apoptosis and necrosis also occur, but ferroptosis highlights the specific role of iron and lipid membranes. Necrotic cell death releases damage-associated molecular patterns (DAMPs) that fuel inflammation, turning localized oxidative damage into systemic immune activation [71].

4.1. Evidence base linking metals to human disease

Mechanistic plausibility is strong, metals contribute to vascular oxidative stress, reduced nitric oxide signaling, inflammation, and autonomic imbalance [72]. Epidemiologic studies of air pollution often implicate metal-rich components or traffic-related particles in cardiovascular endpoints, including hypertension, ischemic events, and changes in heart rate variability [73-75]. Metabolic outcomes, including insulin resistance, may be influenced by oxidative stress in adipose tissue and liver, along with mitochondrial dysfunction. However, causality is complicated by co-pollutants, and improved exposure assessment (metal speciation, source apportionment) is crucial to strengthen inference. Chronic exposure to metal-bearing particles is linked to asthma exacerbations, chronic bronchitis symptoms, and reduced lung function. Metals can impair mucociliary clearance, increase epithelial permeability, and alter immune responses to viruses and bacteria [76]. In susceptible individuals, such as those with asthma, oxidative stress contributes to airway hyperresponsiveness and steroid resistance [77]. Occupational exposures (welding, metal fumes) provide clearer causal evidence, with respiratory symptoms and inflammatory markers correlating with exposure intensity.

Neurotoxicity evidence is strongest for manganese in occupational contexts, where motor symptoms and neurobehavioral changes have been documented [78-809]. For ambient exposure, associations between air pollution and cognitive decline are increasingly studied, and metals may be one component driving neuroinflammation and oxidative injury [81, 82]. The brain's vulnerability to oxidative stress, combined with microglial activation, makes metal contributions plausible, but disentangling metal effects from the broader pollution mixture remains a major research task. Kidney outcomes are relevant for metals that accumulate in renal tissue or cause systemic oxidative stress and vascular dysfunction. Chromium and nickel exposures are classically associated with renal toxicity in certain contexts, while metal-bearing particles can contribute indirectly via inflammation and hypertension [83, 84]. Biomarker-based studies using urine metals alongside renal injury markers (e.g., KIM-1, NGAL) can strengthen exposure-response interpretation [85, 86]. Carcinogenesis pathways include direct genotoxicity (notably Cr(VI)), oxidative DNA damage, chronic inflammation, and epigenetic dysregulation [87]. Nickel and chromium are recognized occupational carcinogens with evidence tied to inhalation exposures [88]. Oxidative stress contributes both by generating mutagenic lesions (8-oxo-dG) and by activating proliferative signaling in chronically inflamed microenvironments [88, 89].

4.2. Measurement and modeling advances: from speciation to the exposome

Speciation defines biological behavior. Cr(VI) versus Cr(III), soluble versus insoluble Ni compounds, and ligand-bound versus labile Fe pools have different uptake and toxicity. Environmental measurements that report only total metal mass can obscure the risk-relevant fraction. Bioaccessibility assays (simulated lung fluid extractions) and advanced spectroscopy (XANES/EXAFS) can reveal chemical forms, while single-particle mass spectrometry can map metal distributions on particle surfaces [90]. Acellular oxidative potential assays (DTT, ascorbate depletion) provide functional measures of particle redox activity [91]. These assays often correlate with metal content and may predict health outcomes better than PM mass alone in some settings. Still, they are simplifications; they do not capture cellular compartmentalization or immune amplification. The best use is as part of a mechanistic framework alongside epidemiology and toxicology. Transcriptomics and epigenomics reveal how metal exposure shifts stress responses, antioxidant defenses, and inflammatory pathways [92]. Single-cell RNA sequencing can identify which lung or immune cell subsets respond most strongly to metal-rich exposures, revealing vulnerability patterns [93]. Proteomics can detect oxidative modifications (carbonylation, adduct formation) and help link chemistry to functional impairment [94].

4.3. Interventions: reducing exposure and restoring redox balance without harming signaling

The most effective intervention is reducing emissions and exposure: cleaner industrial processes, controls on oil combustion emissions, and reductions in traffic-related wear particles. Urban design that lowers near-road exposure and improved occupational protections for welding and metal industries can yield significant health benefits. Indoor air filtration can reduce particle exposure, especially near traffic corridors. For occupational settings, respirators and

ventilation controls are essential. Water infrastructure improvements reduce metal release from pipes and prevent contamination events. Community-based monitoring can identify hotspots for industrial emissions and support targeted policy responses. Because ROS signaling is physiologic, blanket antioxidant therapy has often failed to show consistent benefits in clinical trials. More promising are strategies that target specific pathways:

- **Nrf2 pathway modulation** to enhance endogenous defenses where appropriate,
- **Mitochondria-targeted antioxidants** in contexts of mitochondrial ROS overload,
- **Chelation or binding approaches** in acute high-dose metal exposures under medical supervision,
- **Ferroptosis-targeted protection** (e.g., supporting GPX4 activity, lipid peroxide detoxification) where iron-driven lipid peroxidation dominates.

These approaches require careful risk-benefit evaluation and are not substitutes for exposure reduction.

4.4. Research gaps and future directions

Routine monitoring often reports total metal concentrations without speciation or solubility measures. Future studies should incorporate bioaccessibility and oxidative potential to link exposures to biology more directly. Oxidative stress is compartmentalized. Measuring systemic biomarkers alone may miss localized lung epithelial injury or brain-specific oxidative responses. Multi-compartment sampling and imaging approaches may better capture relevant biology. Metals act with organics, secondary oxidants, and biological agents. Statistical mixture models and experimental mixture designs should become standard, not exceptional. Genetic variation in antioxidant pathways, differences in iron status, and comorbid inflammatory conditions can change risk. Incorporating these modifiers can improve both causal inference and practical risk stratification.Linking metal-driven oxidative biomarkers to hard outcomes (myocardial infarction, CKD progression) remains essential. Longitudinal cohorts with repeated exposure and biomarker assessments, combined with mechanistic work, offer the strongest path.

5. Conclusion

Redox-active metals are distinctive environmental hazards because they can generate oxidants catalytically, amplify inflammatory ROS production, and destabilize redox signaling across critical organs. Their toxicity is governed less by total dose than by chemical form, bioavailability, and the biological compartment where reactions occur. Inhaled metal-bearing particulate matter provides a major exposure route, enabling first-contact chemistry in the lung that propagates systemically through inflammation, endothelial dysfunction, and mitochondrial stress. Disease associations span respiratory and cardiovascular endpoints, neurological outcomes (especially with manganese), kidney injury, and carcinogenesis (notably with Cr(VI)). Advancing the field requires integrating metal speciation, oxidative potential, and mechanistic biomarkers with rigorous epidemiologic designs that address mixtures and susceptibility. The most durable health gains will come from exposure reduction and source control, complemented by targeted, mechanism-informed biological interventions for high-risk groups. In the broader context of environmental health, redox-active metals illustrate a general principle: chemistry at the interface of exposure and biology determines toxicity, and understanding that chemistry is the key to preventing disease.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Schieber M, Chandel NS. ROS function in redox signaling and oxidative stress. Current biology. 2014 May 19;24(10):R453-62.

[2] Costantini D. Understanding diversity in oxidative status and oxidative stress: the opportunities and challenges ahead. Journal of Experimental Biology. 2019 Jul 1;222(13):jeb194688.

[3] Fialkow L, Wang Y, Downey GP. Reactive oxygen and nitrogen species as signaling molecules regulating neutrophil function. Free Radical Biology and Medicine. 2007 Jan 15;42(2):153-64.

[4] Khan M, Ali S, Al Azzawi TN, Saqib S, Ullah F, Ayaz A, Zaman W. The key roles of ROS and RNS as a signaling molecule in plant–microbe interactions. Antioxidants. 2023 Jan 25;12(2):268.

[5] Jomova K, Baros S, Valko M. Redox active metal-induced oxidative stress in biological systems. Transition Metal Chemistry. 2012 Mar;37(2):127-34.

[6] Shul'pin GB, Kozlov YN, Shul'pina LS. Metal complexes containing redox-active ligands in oxidation of hydrocarbons and alcohols: A review. Catalysts. 2019 Dec 9;9(12):1046.

[7] Bachi A, Dalle-Donne I, Scaloni A. Redox proteomics: chemical principles, methodological approaches and biological/biomedical promises. Chemical reviews. 2013 Jan 9;113(1):596-698.

[8] Wu X, Zhou Z, Li K, Liu S. Nanomaterials-induced redox imbalance: challenged and opportunities for nanomaterials in cancer therapy. Advanced Science. 2024 Apr;11(16):2308632.

[9] Valko M, Jomova K, Rhodes CJ, Kuča K, Musílek K. Redox-and non-redox-metal-induced formation of free radicals and their role in human disease. Archives of toxicology. 2016 Jan;90(1):1-37.

[10] Krawic C, Zhitkovich A. Chemical mechanisms of DNA damage by carcinogenic chromium (VI). InAdvances in pharmacology 2023 Jan 1 (Vol. 96, pp. 25-46). Academic Press.

[11] Mezencev R, Gibbons C. Interactions between chromium species and DNA in vitro and their potential role in the toxicity of hexavalent chromium. Metallomics. 2023 Aug;15(8):mfad045.

[12] Peres TV, Schettinger MR, Chen P, Carvalho F, Avila DS, Bowman AB, Aschner M. Manganese-induced neurotoxicity: a review of its behavioral consequences and neuroprotective strategies. BMC Pharmacology and Toxicology. 2016 Nov 4;17(1):57.

[13] Aschner M, Skalny AV, Lu R, Santamaria A, Zhou JC, Ke T, Karganov MY, Tsatsakis A, Golokhvast KS, Bowman AB, Tinkov AA. The role of hypoxia-inducible factor 1 alpha (HIF-1α) modulation in heavy metal toxicity. Archives of Toxicology. 2023 May;97(5):1299-318.

[14] Squadrito GL, Cueto R, Dellinger B, Pryor WA. Quinoid redox cycling as a mechanism for sustained free radical generation by inhaled airborne particulate matter. Free Radical Biology and Medicine. 2001 Nov 1;31(9):1132-8.

[15] Bates JT, Fang T, Verma V, Zeng L, Weber RJ, Tolbert PE, Abrams JY, Sarnat SE, Klein M, Mulholland JA, Russell AG. Review of acellular assays of ambient particulate matter oxidative potential: methods and relationships with composition, sources, and health effects. Environmental science & technology. 2019 Mar 4;53(8):4003-19.

[16] Maciejczyk P, Chen LC, Thurston G. The role of fossil fuel combustion metals in PM2. 5 air pollution health associations. Atmosphere. 2021 Aug 24;12(9):1086.

[17] Roy S, Gupta SK, Prakash J, Habib G, Kumar P. A global perspective of the current state of heavy metal contamination in road dust. Environmental Science and Pollution Research. 2022 May;29(22):33230-51.

[18] Fernandez-Marcos ML. Potentially toxic substances and associated risks in soils affected by wildfires: A review. Toxics. 2022 Jan 11;10(1):31.

[19] Lopez AM, Avila CC, VanderRoest JP, Roth HK, Fendorf S, Borch T. Molecular insights and impacts of wildfire-induced soil chemical changes. Nature Reviews Earth & Environment. 2024 Jun;5(6):431-46.

[20] Omo-Okoro P, Ofori P, Amalapridman V, Dadrasnia A, Abbey L, Emenike C. Soil Pollution and Its Interrelation with Interfacial Chemistry. Molecules. 2025 Jun 18;30(12):2636.\

[21] Chauhan BV, Corada K, Young C, Smallbone KL, Wyche KP. Review on sampling methods and health impacts of fine (PM2. 5,≤ 2.5 μm) and ultrafine (UFP, PM0. 1,≤ 0.1 μm) particles. Atmosphere. 2024 May 7;15(5):572.

[22] Liu Y, Xu F, Liu W, Liu X, Wang D. Characteristics, Sources, Exposure, and Health Effects of Heavy Metals in Atmospheric Particulate Matter. Current Pollution Reports. 2025 Mar 3;11(1):16.

[23] Saini R, Mehra H, Goyal T, Dhiman NK. Dietary antioxidants and their potential role in human disease management. Current Nutrition & Food Science. 2023 Mar 1;19(3):262-81.

[24] Lu A, Li Y, Wang C, Ding H. Interaction between Fe & Mn-bearing minerals and microbes. InIntroduction to Environmental Mineralogy 2023 May 23 (pp. 91-117). Singapore: Springer Nature Singapore.

[25] Hahn L, Vriesen ST, Packroff G, Meier J, Manz W. Anaerobic prokaryotic processes drive manganese release in a drinking water reservoir. Frontiers in Microbiology. 2025 Oct 15;16:1671749.

[26] Zoroddu MA, Aaseth J, Crisponi G, Medici S, Peana M, Nurchi VM. The essential metals for humans: a brief overview. Journal of inorganic biochemistry. 2019 Jun 1;195:120-9.

[27] Mehri A. Trace elements in human nutrition (II)–an update. International journal of preventive medicine. 2020 Jan 1;11(1):2.

[28] Stanislawska M, Halatek T, Cieslak M, Kaminska I, Kuras R, Janasik B, Wasowicz W. Coarse, fine and ultrafine particles arising during welding-Analysis of occupational exposure. Microchemical Journal. 2017 Nov 1;135:1-9.

[29] Junaid M, Hashmi MZ, Malik RN, Pei DS. Toxicity and oxidative stress induced by chromium in workers exposed from different occupational settings around the globe: A review. Environmental Science and Pollution Research. 2016 Oct;23(20):20151-67.

[30] Lin CH, Lai CH, Peng YP, Wu PC, Chuang KY, Yen TY, Xiang YK. Comparative health risk of inhaled exposure to organic solvents, toxic metals, and hexavalent chromium from the use of spray paints in Taiwan. Environmental Science and Pollution Research. 2019 Nov;26(33):33906-16.

[31] Ovalle R. A history of the Fenton reactions (Fenton chemistry for beginners). Reactive Oxygen Species. 2022 Apr 28;1.

[32] Du H, Hu X, Huang Y, Bai Y, Fei Y, Gao M, Li Z. A review of copper-based Fenton reactions for the removal of organic pollutants from wastewater over the last decade: different reaction systems. Environmental Science and Pollution Research. 2024 Apr;31(19):27609-33.

[33] O'Brien PJ, Siraki AG, Shangari N. Aldehyde sources, metabolism, molecular toxicity mechanisms, and possible effects on human health. Critical reviews in toxicology. 2005 Jan 1;35(7):609-62.

[34] Bollineni RC, Hoffmann R, Fedorova M. Proteome-wide profiling of carbonylated proteins and carbonylation sites in HeLa cells under mild oxidative stress conditions. Free Radical Biology and Medicine. 2014 Mar 1;68:186-95.

[35] Jomova K, Alomar SY, Valko R, Nepovimova E, Kuca K, Valko M. The role of redox-active iron, copper, manganese, and redox-inactive zinc in toxicity, oxidative stress, and human diseases. EXCLI journal. 2025 Jul 25;24:880.

[36] Aureliano M, De Sousa-Coelho AL, Dolan CC, Roess DA, Crans DC. Biological consequences of vanadium effects on formation of reactive oxygen species and lipid peroxidation. International journal of molecular sciences. 2023 Mar 11;24(6):5382.

[37] Iskra RY, Fedoruk RS. Chromium, its properties, transformation, and impact on humans. Physiological Journal/Fiziologichnyi Zhurnal. 2022 Jul 1;68(4).

[38] Nyga A, Hart A, Tetley TD. Importance of the HIF pathway in cobalt nanoparticle-induced cytotoxicity and inflammation in human macrophages. Nanotoxicology. 2015 Oct 3;9(7):905-17.

[39] Teschke R. Aluminum, arsenic, beryllium, cadmium, chromium, cobalt, copper, iron, lead, mercury, molybdenum, nickel, platinum, thallium, titanium, vanadium, and zinc: molecular aspects in experimental liver injury. International journal of molecular sciences. 2022 Oct 13;23(20):12213.

[40] Aquilano K, Baldelli S, Ciriolo MR. Glutathione: new roles in redox signaling for an old antioxidant. Frontiers in pharmacology. 2014 Aug 26;5:196.

[41] Georgiou-Siafis SK, Tsiftsoglou AS. The key role of GSH in keeping the redox balance in mammalian cells: mechanisms and significance of GSH in detoxification via formation of conjugates. Antioxidants. 2023 Nov 1;12(11):1953.

[42] Janciauskiene S. The beneficial effects of antioxidants in health and diseases. Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation. 2020 May 22;7(3):182.

[43] Haines DD, Tosaki A. Heme degradation in pathophysiology of and countermeasures to inflammation-associated disease. International journal of molecular sciences. 2020 Dec 18;21(24):9698.

[44] Wang B, Wang Y, Zhang J, Hu C, Jiang J, Li Y, Peng Z. ROS-induced lipid peroxidation modulates cell death outcome: mechanisms behind apoptosis, autophagy, and ferroptosis. Archives of toxicology. 2023 Jun;97(6):1439-51.

[45] Gromadzka G, Tarnacka B, Cieślik M. Aging at the Crossroads of Cuproptosis and Ferroptosis: From Molecular Pathways to Age-Related Pathologies and Therapeutic Perspectives. International Journal of Molecular Sciences. 2026 Jan 4;27(1):522.

[46] Johnson CA, Freyer G, Fabisch M, Caraballo MA, Küsel K, Hochella MF. Observations and assessment of iron oxide and green rust nanoparticles in metal-polluted mine drainage within a steep redox gradient. Environmental Chemistry. 2014 May 19;11(4):377-91.

[47] Wang J, Huang J, Wang L, Chen C, Yang D, Jin M, Bai C, Song Y. Urban particulate matter triggers lung inflammation via the ROS-MAPK-NF-κB signaling pathway. Journal of thoracic disease. 2017 Nov;9(11):4398.

[48] Kaarniranta K, Pawlowska E, Szczepanska J, Jablkowska A, Blasiak J. Role of mitochondrial DNA damage in ROS-mediated pathogenesis of age-related macular degeneration (AMD). International journal of molecular sciences. 2019 May 14;20(10):2374.

[49] West AP, Shadel GS. Mitochondrial DNA in innate immune responses and inflammatory pathology. Nature Reviews Immunology. 2017 Jun;17(6):363-75.

[50] Zuo M, Ye M, Lin H, Liao S, Xing X, Liu J, Wu D, Huang Z, Ren X. Mitochondrial dysfunction in environmental toxicology: mechanisms, impacts, and health implications. Chemical Research in Toxicology. 2024 Nov 1;37(11):1794-806.

[51] Carlstrom M, Montenegro MF. Therapeutic value of stimulating the nitrate-nitrite-nitric oxide pathway to attenuate oxidative stress and restore nitric oxide bioavailability in cardiorenal disease. Journal of internal medicine. 2019 Jan;285(1):2-18.

[52] Cuevas AK, Niu J, Zhong M, Liberda EN, Ghio A, Qu Q, Chen LC. Metal rich particulate matter impairs acetylcholine-mediated vasorelaxation of microvessels in mice. Particle and fibre toxicology. 2015 Jun 4;12(1):14.

[53] Niu J, Liberda EN, Qu S, Guo X, Li X, Zhang J, Meng J, Yan B, Li N, Zhong M, Ito K. The role of metal components in the cardiovascular effects of PM2. 5. PloS one. 2013 Dec 27;8(12):e83782.

[54] Rao X, Zhong J, Brook RD, Rajagopalan S. Effect of particulate matter air pollution on cardiovascular oxidative stress pathways. Antioxidants & redox signaling. 2018 Mar 20;28(9):797-818.

[55] Liu L, Urch B, Szyszkowicz M, Evans G, Speck M, Van Huang A, Leingartner K, Shutt RH, Pelletier G, Gold DR, Brook JR. Metals and oxidative potential in urban particulate matter influence systemic inflammatory and neural biomarkers: A controlled exposure study. Environment international. 2018 Dec 1;121:1331-40.

[56] Ding R, Huang L, Yan K, Sun Z, Duan J. New insight into air pollution-related cardiovascular disease: an adverse outcome pathway framework of PM2. 5-associated vascular calcification. Cardiovascular Research. 2024 May;120(7):699-707.

[57] Bondy SC. Metal toxicity and neuroinflammation. Current Opinion in Toxicology. 2021 Jun 1;26:8-13.

[58] Harischandra DS, Ghaisas S, Zenitsky G, Jin H, Kanthasamy A, Anantharam V, Kanthasamy AG. Manganese-induced neurotoxicity: new insights into the triad of protein misfolding, mitochondrial impairment, and neuroinflammation. Frontiers in neuroscience. 2019 Jun 26;13:654.

[59] Ijomone OK, Ukwubile II, Aneke VO, Olajide TS, Inyang HO, Omotosho OI, Oyerinde TO, Anadu VE, Gbayisomore TJ, Okeowo OM, Oyeniran DA. Glial perturbation in metal neurotoxicity: implications for brain disorders. Neuroglia. 2025 Jan 6;6(1):4.

[60] Adhikary S, Saha J, Dutta P, Pal A. Bacterial homeostasis and tolerance to potentially toxic metals and metalloids through diverse transporters: metal-specific insights. Geomicrobiology Journal. 2024 May 2;41(5):496-518.

[61] Mishra M, Nichols L, Dave AA, Pittman EH, Cheek JP, Caroland AJ, Lotwala P, Drummond J, Bridges CC. Molecular mechanisms of cellular injury and role of toxic heavy metals in chronic kidney disease. International Journal of Molecular Sciences. 2022 Sep 21;23(19):11105.

[62] Chevalier RL. The proximal tubule is the primary target of injury and progression of kidney disease: role of the glomerulotubular junction. American Journal of Physiology-Renal Physiology. 2016 Jul 1;311(1):F145-61.

[63] Winterbourn CC, Kettle AJ, Hampton MB. Reactive oxygen species and neutrophil function. Annual review of biochemistry. 2016 Jun 2;85(1):765-92.

[64] Shen G, Jeong WS, Hu R, Kong AN. Regulation of Nrf2, NF-κB, and AP-1 signaling pathways by chemopreventive agents. Antioxidants & redox signaling. 2005 Nov 1;7(11-12):1648-63.

[65] Buelna-Chontal M, Zazueta C. Redox activation of Nrf2 & NF-κB: a double end sword?. Cellular signalling. 2013 Dec 1;25(12):2548-57.

[66] Chervona Y, Costa M. The control of histone methylation and gene expression by oxidative stress, hypoxia, and metals. Free radical biology and medicine. 2012 Sep 1;53(5):1041-7.

[67] Hernández-Cruz EY, Arancibia-Hernández YL, Loyola-Mondragón DY, Pedraza-Chaverri J. Oxidative stress and its role in Cd-induced epigenetic modifications: use of antioxidants as a possible preventive strategy. Oxygen. 2022 May 29;2(2):177-210.

[68] Dar NJ, John U, Bano N, Khan S, Bhat SA. Oxytosis/ferroptosis in neurodegeneration: the underlying role of master regulator glutathione peroxidase 4 (GPX4). Molecular neurobiology. 2024 Mar;61(3):1507-26.\

[69] Wang B, Wang Y, Zhang J, Hu C, Jiang J, Li Y, Peng Z. ROS-induced lipid peroxidation modulates cell death outcome: mechanisms behind apoptosis, autophagy, and ferroptosis. Archives of toxicology. 2023 Jun;97(6):1439-51.

[70] Shen Y, Zhang G, Wei C, Zhao P, Wang Y, Li M, Sun L. Potential role and therapeutic implications of glutathione peroxidase 4 in the treatment of Alzheimer's disease. Neural Regeneration Research. 2025 Mar 1;20(3):613-31.

[71] Land WG. The role of damage-associated molecular patterns (DAMPs) in human diseases: part II: DAMPs as diagnostics, prognostics and therapeutics in clinical medicine. Sultan Qaboos University Medical Journal. 2015 May 28;15(2):e157.

[72] Rajpoot A, Aggarwal T, Sharma V. Unraveling the enigma of cardiac damage caused by lead: Understanding the intricate relationship between oxidative stress and other multifactorial mechanisms. Toxicology. 2024 Dec 1;509:153984.

[73] Brook RD, Rajagopalan S, Pope III CA, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation. 2010 Jun 1;121(21):2331-78.

[74] Miller MR, Shaw CA, Langrish JP. From particles to patients: oxidative stress and the cardiovascular effects of air pollution. Future cardiology. 2012 Jul 1;8(4):577-602.

[75] Miller MR, Landrigan PJ, Arora M, Newby DE, Münzel T, Kovacic JC. Environmentally not so friendly: global warming, air pollution, and wildfires: JACC focus seminar, part 1. Journal of the American College of Cardiology. 2024 Jun 11;83(23):2291-307.

[76] Alekseenko SI, Skalny AV, Ajsuvakova OP, Skalnaya MG, Notova SV, Tinkov AA. Mucociliary transport as a link between chronic rhinosinusitis and trace element dysbalance. Medical Hypotheses. 2019 Jun 1;127:5-10.

[77] Enweasor C, Flayer CH, Haczku A. Ozone-induced oxidative stress, neutrophilic airway inflammation, and glucocorticoid resistance in asthma. Frontiers in Immunology. 2021 Feb 26;12:631092.

[78] Roels HA, Bowler RM, Kim Y, Henn BC, Mergler D, Hoet P, Gocheva VV, Bellinger DC, Wright RO, Harris MG, Chang Y. Manganese exposure and cognitive deficits: a growing concern for manganese neurotoxicity. Neurotoxicology. 2012 Aug 1;33(4):872-80.

[79] Peres TV, Schettinger MR, Chen P, Carvalho F, Avila DS, Bowman AB, Aschner M. Manganese-induced neurotoxicity: a review of its behavioral consequences and neuroprotective strategies. BMC Pharmacology and Toxicology. 2016 Nov 4;17(1):57.

[80] Martin KV, Edmondson D, Cecil KM, Bezi C, Vance ML, McBride D, Haynes EN. Manganese exposure and neurologic outcomes in adult populations. Neurologic clinics. 2020 Nov 1;38(4):913-36.

[81] Jayaraj RL, Rodriguez EA, Wang Y, Block ML. Outdoor ambient air pollution and neurodegenerative diseases: the neuroinflammation hypothesis. Current environmental health reports. 2017 Jun;4(2):166-79.

[82] Hahad O, Lelieveld J, Birklein F, Lieb K, Daiber A, Münzel T. Ambient air pollution increases the risk of cerebrovascular and neuropsychiatric disorders through induction of inflammation and oxidative stress. International journal of molecular sciences. 2020 Jun 17;21(12):4306.

[83] Boffetta P, Fontana L, Stewart P, Zaridze D, Szeszenia-Dabrowska N, Janout V, Bencko V, Foretova L, Jinga V, Matveev V, Kollarova H. Occupational exposure to arsenic, cadmium, chromium, lead and nickel, and renal cell carcinoma: a case–control study from Central and Eastern Europe. Occupational and environmental medicine. 2011 Oct 1;68(10):723-8.

[84] Moody EC, Coca SG, Sanders AP. Toxic metals and chronic kidney disease: a systematic review of recent literature. Current environmental health reports. 2018 Dec;5(4):453-63.

[85] Vrijheid M, Slama R, Robinson O, Chatzi L, Coen M, Van den Hazel P, Thomsen C, Wright J, Athersuch TJ, Avellana N, Basagaña X. The human early-life exposome (HELIX): project rationale and design. Environmental health perspectives. 2014 Mar 7;122(6):535.

[86] Hong S, Zhang Y, Hu G, Jia G. Exploration of whole blood chromium as biomarker of hexavalent chromium exposure: based on literature review and Monte Carlo simulation. Biological Trace Element Research. 2023 May;201(5):2274-83.

[87] Salnikow K, Zhitkovich A. Genetic and epigenetic mechanisms in metal carcinogenesis and cocarcinogenesis: nickel, arsenic, and chromium. Chemical research in toxicology. 2008 Jan 21;21(1):28-44.

[88] Zhao L, Islam R, Wang Y, Zhang X, Liu LZ. Epigenetic regulation in chromium-, nickel-and cadmium-induced carcinogenesis. Cancers. 2022 Nov 23;14(23):5768.

[89] Krawic C, Zhitkovich A. Chemical mechanisms of DNA damage by carcinogenic chromium (VI). InAdvances in pharmacology 2023 Jan 1 (Vol. 96, pp. 25-46). Academic Press.

[90] Guilherme Buzanich A. Recent developments of X-ray absorption spectroscopy as analytical tool for biological and biomedical applications. X-Ray Spectrometry. 2022 May;51(3):294-303.

[91] Bates JT, Fang T, Verma V, Zeng L, Weber RJ, Tolbert PE, Abrams JY, Sarnat SE, Klein M, Mulholland JA, Russell AG. Review of acellular assays of ambient particulate matter oxidative potential: methods and relationships with composition, sources, and health effects. Environmental science & technology. 2019 Mar 4;53(8):4003-19.

[92] Hernández-Cruz EY, Arancibia-Hernández YL, Loyola-Mondragón DY, Pedraza-Chaverri J. Oxidative stress and its role in Cd-induced epigenetic modifications: use of antioxidants as a possible preventive strategy. Oxygen. 2022 May 29;2(2):177-210.

[93] Bi F, Gao C, Guo H. Epigenetic regulation of cardiovascular diseases induced by behavioral and environmental risk factors: Mechanistic, diagnostic, and therapeutic insights. FASEB BioAdvances. 2024 Nov;6(11):477-502.

[94] Baraibar MA, Ladouce R, Friguet B. Proteomic quantification and identification of carbonylated proteins upon oxidative stress and during cellular aging. Journal of proteomics. 2013 Oct 30;92:63-70.