VDM VASCULAR DISEASE MANAGEMENT
OFFICIAL MEDIA PARTNER OF iSET | AMP

LITERATURE REVIEW

PEER REVIEWED

Microplastics as Triggers of Immunothrombosis: Linking Environmental Exposure to Cardiovascular Events

Abiya Ahad, MBBS
Darshan Hullon, DO

Keywords
Microplastics
Nanoplastics
Immunothrombosis
Endothelial Dysfunction
NLRP3 Inflammasome
Cardiovascular Disease

May 2026
ISSN 2152-4343

Key Summary

- Review summarizes mechanistic, translational, and limited human observational evidence linking microplastic/nanoplastic (MP/NP) exposure (via ingestion, inhalation, and medical sources) to cardiovascular immunothrombosis; MPs have been detected in blood, thrombi, and atherosclerotic plaques.
- Key findings indicate that MP/NP exposure promotes endothelial injury, NLRP3 inflammasome activation, platelet activation, NETosis, and coagulation pathway dysregulation, creating a proatherothrombotic state; a cited human plaque study reports an approximately 4.5-fold higher risk of myocardial infarction, stroke, or death over 34 months in patients with detectable plaque MPs.
- Clinically, MPs may act as cardiovascular risk amplifiers and potential therapeutic targets (eg, anti-inflammatory pathways), but interpretation is limited by particle heterogeneity, lack of standardized detection methods, and uncertain dose–response relationships, highlighting the need for prospective exposome-based studies.

VASCULAR DISEASE MANAGEMENT. 2026;23(5):E58-E69

Abstract

The emergence of microplastics (MPs) and nanoplastics (NPs) as pervasive environmental contaminants has introduced a novel and mechanistically complex dimension to cardiovascular risk. Beyond their physical ubiquity, these particles engage biological systems through surface chemistry, adsorbed toxicants, and size-dependent cellular uptake, collectively generating a proatherothrombotic milieu. This narrative review synthesizes current mechanistic, translational, and clinical evidence linking environmental MP/NP exposure to immunothrombosis—a pathophysiological process in which innate immune activation and the coagulation cascade mutually amplify, driving vascular disease. In this review, we delineate how ingested, inhaled, and iatrogenically introduced particles breach biological barriers, enter systemic circulation, and engage endothelial cells, monocytes, macrophages, neutrophils, and platelets through oxidative, inflammatory, and mechanosensory mechanisms. Special attention is paid to NLRP3 inflammasome activation, neutrophil extracellular trap formation, glycocalyx erosion, and coagulation factor dysregulation as convergent pathways linking particle exposure to atherosclerosis, plaque instability, myocardial infarction, stroke, and microvascular dysfunction. We further examine the "Trojan horse" function of MPs as vectors for adsorbed heavy metals, persistent organic pollutants, and endocrine-disrupting chemicals, which synergistically amplify vascular toxicity. Human biomonitoring data confirming MP detection in blood, thrombi, and atherosclerotic plaques are critically appraised for their epidemiological associations with incident cardiovascular events. Methodological limitations, including particle heterogeneity, absence of standardized detection protocols, and dose-response uncertainty, are examined, and a research agenda integrating exposomics, in vivo imaging, and therapeutic targeting is proposed.

Introduction and Framing Within the Cardiovascular Exposome

The concept of the exposome—the totality of environmental exposures across a lifetime—has reshaped how cardiovascular epidemiologists conceptualize risk beyond classical Framingham variables.[1] Air pollution, heavy metals, endocrine-disrupting chemicals, and persistent organic pollutants have each been integrated into this framework as cardiotoxic stressors. Microplastics (MPs) and nanoplastics (NPs) now demand similar recognition. Defined by convention as synthetic polymer particles below 5 mm in diameter, MPs encompass a chemically and morphologically diverse ensemble: polyethylene (PE), polypropylene (PP), polystyrene (PS), polyethylene terephthalate (PET), polyvinyl chloride, and polyfluoroalkyl-containing polymers are among the most prevalent. In contrast, NPs, operationally defined as particles smaller than 1 µm, increasingly command mechanistic interest due to their ability to traverse epithelial and endothelial barriers and enter subcellular compartments.[2,3] Global annual plastic production exceeded 400 million metric tons as of 2022, and the fragmentation of macroplastics through photodegradation, mechanical abrasion, and biological weathering leads to exponential accumulation of smaller particles in terrestrial, aquatic, and atmospheric reservoirs.[4] Crucially, MPs and NPs have now been detected in the human lung, liver, kidney, placenta, breast milk, and—most relevant for cardiovascular medicine—the systemic bloodstream and within atherosclerotic plaques.[5,6]

What distinguishes MPs and NPs from other environmental toxicants is not merely their prevalence but their biological versatility. Their high surface-area-to-volume ratio facilitates adsorption of hydrophobic organic chemicals, including polychlorinated biphenyls, polycyclic aromatic hydrocarbons (PAHs), phthalates, bisphenols, heavy metals such as cadmium and lead, and per- and poly-fluoroalkyl substances (PFAS), effectively transforming each particle into a concentrated vector of co-toxicants.[7] As cardiovascular medicine increasingly engages with the biological complexity of environmental exposures,[8,9] MPs merit positioning not as isolated pollutants but as multifunctional cardiovascular risk amplifiers capable of driving immunothrombotic disease through converging molecular pathways.

Routes of Exposure and Translocation Into Systemic Circulation

Human exposure to MPs and NPs is continuous and occurs via multiple converging routes, each with distinct translocation dynamics. Dietary ingestion represents the highest-volume route, with estimates ranging from 39,000 to more than 52,000 particles per person per year depending on water consumption and food packaging habits. However, methodological inconsistencies across studies make precise quantification difficult.[10] MPs are present in bottled and tap water, seafood, table salt, honey, beer, and processed foods, and NPs leach from plastic food containers, particularly under thermal stress. Following ingestion, particle uptake across the gastrointestinal epithelium proceeds through multiple mechanisms.

Enterocytes efficiently endocytose particles below 150 nm via clathrin- and caveolae-mediated pathways, whereas larger particles, up to 5 to 10 µm, are preferentially taken up by intestinal microfold cells overlying Peyer's patches, a well-characterized route exploited by enteric pathogens.[11] Following transcytosis, particles enter mesenteric lymphatics and subsequently the portal and systemic circulation, a translocation sequence now confirmed by detection of PS and PE particles in human portal blood and hepatic tissue.[5]

Inhalation constitutes a quantitatively significant and mechanistically important secondary route. Airborne MPs, generated from synthetic textile fibers, tire wear particles, and building materials, deposit in the bronchial and alveolar mucosa proportional to aerodynamic diameter. Particles below 2.5 µm reach the alveolar space, where submicrometer and nanoscale particles are taken up by alveolar macrophages or translocate directly across the thin alveolar–capillary membrane into the pulmonary circulation.[12] Occupational settings such as textile manufacturing, plastic recycling, and synthetic rubber production expose workers to substantially higher MP burdens, and elevated urinary phthalate and bisphenol metabolites in these populations correlate with endothelial dysfunction biomarkers.[13] The dermal route, while quantitatively less significant for internal exposure, gains relevance in the context of cosmetics containing microbeads—now banned in several jurisdictions—and in clinical settings where plasticizer leaching from polyvinyl chloride intravenous tubing, catheters, and blood bags introduces DEHP and other plasticizers directly into the vasculature of hospitalized patients.[14] This iatrogenic exposure pathway warrants renewed attention, given the breadth of plastic-containing medical devices used in contemporary critical care and interventional practice.[15]

Once in systemic circulation, the fate of MPs is governed by size, surface charge, and polymer hydrophobicity. Smaller particles circulate as free entities or associate with plasma proteins forming a "protein corona" that alters surface reactivity, modulates cellular uptake, and may disguise particle identity from innate immune recognition.[16] Larger circulating particles are captured by hepatic Kupffer cells, splenic macrophages, and pulmonary intravascular macrophages, generating localized inflammatory foci. Importantly, circulating NPs have been shown to directly engage the vascular endothelium, initiating a cascade of endothelial injury that underpins the immunothrombotic response detailed below.[17]

Endothelial Dysfunction and Glycocalyx Disruption

The vascular endothelium, a metabolically active monolayer lining more than 60,000 km of vasculature, is both the first contact surface for circulating MPs and the critical gatekeeper of thrombotic homeostasis. Under physiological conditions, the endothelial glycocalyx—a structured network of heparan sulfate proteoglycans, chondroitin sulfates, hyaluronan, and associated plasma proteins—projects 0.5 to 3 μm into the luminal space and serves as a mechanosensor, a charge barrier against leukocyte adhesion, and a reservoir for antithrombotic mediators including antithrombin III, tissue factor pathway inhibitor, and nitric oxide synthase.[18] Experimental models consistently demonstrate that PS-NPs and PE-MPs at concentrations plausible for human exposure induce dose-dependent shedding of glycocalyx components, including syndecan-1, heparan sulfate, and hyaluronic acid, measurable both in supernatants of particle-exposed endothelial cell cultures and in plasma of MP-exposed rodents.[19] Mechanistically, glycocalyx erosion is driven by reactive oxygen species (ROS)-mediated activation of heparanase and matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, whose catalytic activity is amplified by the inflammatory cytokine milieu generated downstream of particle uptake.[20]

Glycocalyx disruption creates a self-reinforcing cycle of endothelial vulnerability. Exposure of underlying adhesion molecules—intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1, and E-selectin—facilitates leukocyte rolling and firm adhesion, while reduced endothelial nitric oxide synthase (eNOS) activity consequent to glycocalyx loss impairs vasodilation and permits unopposed vasoconstriction. In parallel, translocation of tissue factor (TF) from the abluminal to the luminal endothelial surface following glycocalyx disruption creates a procoagulant nidus capable of initiating the extrinsic coagulation pathway.[21] Flow-disturbed regions at arterial bifurcations, where shear stress is already low and oscillatory, appear disproportionately vulnerable to MP-induced glycocalyx erosion, providing a mechanistic basis for the predilection of atherosclerosis and thrombosis to these anatomical sites.[22] Beyond glycocalyx perturbation, endothelial cells exposed to PS-NPs exhibit reduced transendothelial electrical resistance—a functional correlate of barrier integrity—associated with disruption of the tight junction proteins occludin and claudin-5 via activation of RhoA/Rho-associated protein kinase signaling, thereby enabling transcellular and paracellular particle trafficking.[23]

Oxidative Stress and Mitochondrial Injury

Central to the pathophysiology of MP-induced vascular toxicity is the generation of oxidative stress, which serves as a molecular hub integrating particle-driven cellular injury, inflammatory activation, and thrombogenic signaling. ROS production in response to MPs and NPs arises from multiple convergent sources: direct photocatalytic activity of certain particle surfaces, uncoupling of mitochondrial electron transport chain complexes, activation of NADPH oxidase (NOX) isoforms, particularly NOX2 and NOX4, in endothelial cells and monocytes, and depletion of cellular antioxidant reserves, including glutathione and superoxide dismutase.[24] In vitro studies with PS-NPs demonstrate mitochondrial membrane potential collapse, cytochrome c release, and induction of the intrinsic apoptotic pathway in human umbilical vein endothelial cells at concentrations in the microgram-per-milliliter range.[25] These mitochondrial effects are particularly relevant because mitochondrial dysfunction activates the NLRP3 inflammasome through the cytoplasmic release of mitochondrial DNA and cardiolipin, which serve as damage-associated molecular patterns sensed by the innate immune system.[26]

The relevance of heavy metal co-exposure cannot be overstated in this context. MPs adsorb cadmium, lead, arsenic, and chromium at concentrations several orders of magnitude above ambient water levels.[7] Cadmium, a well-established cardiovascular toxicant, shares mechanistic pathways with MPs: it induces mitochondrial dysfunction, increases NOX-derived superoxide production, and impairs eNOS coupling, thereby converting eNOS from an NO producer to a superoxide generator—a state termed eNOS uncoupling that amplifies endothelial injury.[27] A systematic review specifically examining cobalt-induced cardiomyopathy demonstrated that mitochondrial dysfunction and oxidative stress are central to metal-induced cardiac toxicity, with reversible impairment of respiratory chain complexes I and III as key molecular events.[28] This mechanistic convergence between metal toxicology and MP-mediated vascular injury suggests that the cardiovascular hazard of environmental MPs is materially amplified by their role as metal delivery vehicles, particularly in populations with high dietary or occupational metal exposure.[7]

Oxidative stress from MP exposure further promotes lipid peroxidation, generating 4-hydroxynonenal and malondialdehyde, which form adducts with apolipoprotein B, thereby enhancing low-density lipoprotein (LDL) oxidizability and foam cell formation. Isoprostane species generated through non-enzymatic oxidation of arachidonic acid activate thromboxane A2 receptors on platelets, promoting aggregation independent of traditional platelet agonists.[29] Thus, oxidative stress integrates MP exposure with both the atherogenic and thrombogenic limbs of cardiovascular disease through biochemically distinct but interlinked mechanisms.

Innate Immune Activation: Macrophages, Monocytes, and the NLRP3 Inflammasome

The innate immune response to circulating MPs engages myeloid cells—monocytes, macrophages, and dendritic cells—via pattern recognition receptors that recognize these particles as sterile danger signals. Toll-like receptors (TLRs), particularly TLR4, recognize hydrophobic surface motifs on PS particles and initiate MyD88-dependent NF-κB signaling, driving transcription of pro-inflammatory cytokines including interleukin-1β (IL-1β), IL-6, IL-8, and tumor necrosis factor-α (TNF-α).[30] Macrophages exposed to MP internalize particles through phagocytosis and macropinocytosis; however, particles exceeding the phagocytic capacity of a single macrophage—typically those above 10 μm—induce frustrated phagocytosis, a state characterized by sustained degranulation and lysosomal membrane permeabilization without successful engulfment, closely analogous to the macrophage response to monosodium urate crystals in gout.[31]

Lysosomal damage consequent to phagocytosed MP-induced mechanical stress releases cathepsin B into the cytoplasm, a critical signal activating the NLRP3 inflammasome complex. NLRP3 inflammasome assembly (integrating NLRP3 sensor, ASC adaptor, and procaspase-1) leads to caspase-1 activation, proteolytic maturation of pro-IL-1β and pro-IL-18, and gasdermin D cleavage with pyroptotic pore formation.[32] IL-1β drives monocyte recruitment, promotes macrophage differentiation toward the M1 pro-inflammatory phenotype, stimulates hepatic acute-phase protein synthesis, and activates the coagulation cascade by upregulating tissue factor expression on monocytes and endothelial cells. IL-18 promotes interferon-γ production from natural killer cells and T cells, amplifying the vascular inflammatory response. In murine models, PS-MP gavage induces hepatic and systemic IL-1β elevation, macrophage infiltration into the aortic adventitia, and accelerated atherosclerotic lesion development in apolipoprotein E (ApoE)-deficient mice, effects that are abrogated by the NLRP3 inhibitor MCC950.33 These experimental findings position NLRP3 inflammasome activation as a mechanistically pivotal link between MP exposure and atheroinflammation, with therapeutic implications discussed subsequently.

Circulating classical monocytes (CD14++CD16-) respond to MP-derived signals by upregulating CCR2 and CX3CR1, facilitating transendothelial migration into inflamed plaque. Once within the subintimal space, monocyte-derived macrophages ingest oxidized LDL through scavenger receptors SR-A and CD36, generating lipid-laden foam cells—the histological hallmark of early atherosclerotic lesions. Critically, MP particles have been detected within foam cells in experimental atherosclerotic lesions, suggesting that particles themselves, rather than solely their soluble mediators, participate directly in lesion biology.[34] Classical monocytes from MP-exposed individuals exhibit epigenetic reprogramming consistent with trained immunity (a form of non-specific memory in innate immune cells mediated by histone methylation changes at inflammatory gene loci), potentially sustaining a pro-inflammatory monocyte phenotype long after particle exposure and contributing to chronic cardiovascular risk elevation.[35]

Platelet Activation and Aggregation Pathways

Platelets, anucleate cytoplasmic fragments shed from megakaryocytes, are exquisitely sensitive biosensors of endovascular injury and serve as primary effectors of thrombosis. Their activation by MPs occurs through multiple surface receptor-mediated and receptor-independent pathways. Direct contact of circulating PS and PE particles with platelet membranes elicits rapid calcium influx, dense granule release of ADP and serotonin, and alpha granule secretion of von Willebrand factor (vWF), P-selectin, and fibrinogen, creating a self-amplifying activation cascade.[36]

Mechanistically, MP surface hydrophobicity promotes non-specific protein adsorption, including vWF and fibrinogen, which undergo conformational changes upon adsorption, exposing cryptic platelet-binding epitopes and effectively mimicking the conditions of vascular injury. Immobilized vWF binds platelet glycoprotein Ibα under high shear conditions, providing the initial tethering force analogous to subendothelial collagen exposure in classical thrombosis.[37]

Beyond direct contact effects, the upstream pro-inflammatory cytokine milieu amplifies platelet reactivity: TNF-α sensitizes platelets via TNFR1-mediated signaling, IL-1β promotes thrombopoiesis and platelet hyperreactivity, and thromboxane A2, generated from arachidonic acid liberated by phospholipase A2 in inflammatory cells, acts as a potent platelet agonist. ROS generated by NADPH oxidase in MP-exposed endothelial cells and monocytes oxidize platelet membrane lipids, activating scramblase and externalizing phosphatidylserine (PS-exposure), which provides a catalytic surface for coagulation complex assembly.[38] Platelet-rich thrombi are further stabilized by cross-linking of fibrin generated through the coagulation cascade, and the net effect is a platelet–fibrin thrombus architecturally indistinguishable from that observed in acute coronary syndrome, suggesting that MPs can authentically recapitulate the thrombogenic milieu of plaque rupture through an entirely endogenous mechanism.[39] The peripheral vascular implications of platelet hyperactivation and thrombotic occlusion in this context are directly relevant to outcomes in patients with established arterial disease, where flow restoration through endovascular interventions remains the cornerstone of limb salvage therapy.[15,40]

NETosis and Neutrophil-Mediated Thrombosis

Neutrophils, the most abundant circulating leukocytes, contribute to immunothrombosis through their capacity to form neutrophil extracellular traps (NETs)—web-like structures of decondensed chromatin decorated with citrullinated histones, neutrophil elastase, myeloperoxidase (MPO), and antimicrobial peptides. NET formation, or NETosis, was originally characterized as an antimicrobial defense but has emerged as a central driver of pathological thrombosis in settings including sepsis, antiphospholipid syndrome, COVID-19, and myocardial infarction.[41] Compelling experimental data now demonstrate that MPs induce NETosis through multiple convergent pathways. PS-NPs at nanomolar surface concentrations activate toll-like receptor 2/4 signaling on neutrophils, triggering peptidylarginine deiminase 4 (PAD4)-dependent citrullination of histone H3 and subsequent chromatin decondensation required for NET extrusion.[42] Independently, ROS generated by NADPH oxidase within the neutrophil phagolysosome drives oxidative NETosis via activation of PAD4.

NETs contribute to thrombosis through multiple mechanisms: citrullinated histone H3 directly activates platelets and endothelial cells; released DNA provides a scaffold for platelet adhesion and thrombin generation; neutrophil elastase and MPO proteolytically inactivate tissue factor pathway inhibitor and activate factor XII; and NETs promote erythrocyte retention within thrombi, generating the compact red thrombus architecture characteristic of venous thromboembolism. Importantly, NET markers—cell-free DNA, citrullinated H3, MPO–DNA complexes—are elevated in venous thromboembolism, a condition for which treatment with direct oral anticoagulants has been increasingly studied across diverse patient populations, including those with obesity.[43] The MP–NETosis axis thus provides a biological basis for the previously unexplained epidemiological association between environmental pollution and venous thrombotic events, complementing established arterial thrombosis mechanisms.[44] Furthermore, NET-embedded MPs can serve as inflammatory amplifiers: the dense chromatin scaffold concentrates MP-adsorbed toxicants at endothelial contact points, creating local high-dose toxicant exposure exceeding what free-floating particles would achieve in the same vascular microenvironment.[45]

Coagulation Cascade Activation and Fibrin Remodeling

The coagulation cascade intersects with MP-driven immunothrombosis at multiple levels beyond platelet activation and NETosis. TF, the primary initiator of the extrinsic coagulation pathway, is upregulated on monocytes, macrophages, and endothelial cells by the NF-κB-driven inflammatory response to MPs, and TF-bearing microparticles shed from activated cells further propagate coagulation activation throughout the circulation.[46] Factor XII (FXII), the initiator of the contact activation pathway, adsorbs avidly to negatively charged MP surfaces—particularly carboxylated or oxidized polymers—and undergoes autoactivation, analogous to its behavior on kaolin or glass surfaces used in clinical coagulation testing.[47] FXII activation generates FXIIa, which activates FXI and, ultimately, thrombin, thereby cleaving fibrinogen to fibrin. Notably, FXII-initiated coagulation also generates bradykinin through the kallikrein–kinin system, inducing endothelial permeability and inflammatory pain signaling that may contribute to clinical microvascular dysfunction.[48]

Fibrin formed within MP-containing thrombi exhibits structural alterations attributable to direct polymer–fibrin interactions. PS particles incorporated within forming fibrin clots produce thinner, more densely packed fiber networks with increased clot stiffness and reduced fibrinolytic susceptibility, as assessed by viscoelastic hemostatic assays and scanning electron microscopy of in vitro clot models.[49] This fibrin remodeling represents a potentially clinically significant mechanism by which MPs impair thrombolysis (the primary pharmacological strategy in acute ischemic stroke and ST-elevation myocardial infarction), suggesting that elevated circulating MP burden may contribute to resistance to fibrinolytic therapy. Additionally, plasminogen activator inhibitor-1, the primary inhibitor of tissue plasminogen activator and urokinase, is upregulated by inflammatory cytokines (particularly IL-1β and TNF-α) as well as by ROS and endoplasmic reticulum stress, all of which are activated by MP exposure, further tilting the hemostatic balance toward fibrin preservation and thrombus persistence.[50]

Microplastics as Vectors for Adsorbed Toxins, Heavy Metals, and Endocrine Disruptors

A mechanistic discussion of MP cardiovascular toxicity would be incomplete without detailed treatment of their role as environmental concentrators and delivery vehicles. The high surface area and hydrophobic surface chemistry of MPs—particularly PE, PP, and PS—creates thermodynamic conditions favoring adsorption of organic compounds at concentrations up to 10^6-fold above ambient water levels.[7] PAHs adsorbed to MPs are efficiently transferred to biological tissues upon particle ingestion; following desorption in the lipid-rich intestinal environment, PAHs undergo cytochrome P450-mediated bioactivation to reactive arene oxides and diol epoxides that form DNA adducts, activate the aryl hydrocarbon receptor (AhR), and stimulate production of inflammatory mediators and pro-oxidant enzymes.[51] AhR activation in endothelial cells induces CYP1B1 expression, which converts estradiol to 4-hydroxyestradiol, a catechol estrogen that generates superoxide through redox cycling—linking MP-adsorbed PAHs to endothelial oxidative stress through an indirect but biologically potent mechanism.[52]

Phthalates and bisphenol A (BPA), ubiquitous plasticizers and monomers that leach from MPs in biological fluids, are established endocrine disruptors with cardiovascular relevance. Di(2-ethylhexyl)phthalate (DEHP) metabolites, particularly mono(2-ethylhexyl)phthalate, activate peroxisome proliferator-activated receptor α (PPARα) and PPARγ in cardiomyocytes and vascular smooth muscle cells, altering lipid metabolism and promoting foam cell formation.[53] BPA at picomolar concentrations activates estrogen receptor β in cardiac myocytes, inducing arrhythmogenic calcium handling abnormalities, and promotes macrophage polarization toward the M1 inflammatory phenotype through suppression of IL-10 and enhancement of IL-12 secretion.[54] PFAS compounds, increasingly detected as MP surface contaminants, activate NF-κB and suppress PPARγ in macrophages, promoting cholesterol crystal formation and amplifying NLRP3 inflammasome-dependent IL-1β release.[55] The clinical relevance of these endocrine-disrupting co-toxicants is underscored by large epidemiological studies demonstrating that urinary phthalate metabolite concentrations are independently associated with elevated high-sensitivity C-reactive protein, carotid intima-media thickness progression, and incident cardiovascular events, even after adjustment for direct MP exposure metrics.[56]

Clinical Cardiovascular Outcomes: From Atherosclerosis to Acute Events

The mechanistic pathways described converge on recognizable clinical cardiovascular phenotypes. Atherosclerosis, the fundamental substrate for most major adverse cardiovascular events, is driven by the intersection of lipid retention, endothelial activation, monocyte recruitment, and foam cell accumulation—processes that MP exposure accelerates through complementary mechanisms. In ApoE-/- and low-density lipoprotein receptor -/- murine models fed high-fat diets and exposed to oral PS-MPs, lesion area in the aortic root increases significantly compared with unexposed controls, and lesion composition shifts toward a more vulnerable phenotype characterized by larger necrotic cores, thinner fibrous caps, and greater macrophage density.[33] These histological changes, collectively constituting plaque vulnerability by established criteria, are driven by the synergistic actions of NLRP3-dependent IL-1β, oxidized LDL, and NET-mediated matrix degradation, which together impair the efferocytic capacity of plaque macrophages and promote apoptotic cell accumulation.[57]

The transition from stable plaque to acute coronary event involves fibrous cap disruption or superficial plaque erosion, with subsequent thrombus formation. MPs, by amplifying platelet reactivity, promoting NET formation, and activating the contact coagulation pathway, could both destabilize vulnerable plaques through MMP-mediated matrix degradation and create a hypercoagulable luminal environment facilitating occlusive thrombus propagation after minimal plaque disruption.[58] This dual mechanism (plaque vulnerability promotion combined with enhanced thrombogenicity) potentially explains why environmental air pollution, a surrogate exposure for inhaled MPs and particle matter, is associated with incident myocardial infarction with effect sizes disproportionate to its moderate inflammatory signal in isolation.[59] The downstream clinical and health-economic consequences of acute coronary events and ischemic strokes, including costs of mechanical thrombectomy, post-acute care, and cardiac rehabilitation, represent a substantial and growing societal burden[8,9] that MP-related cardiovascular disease stands to amplify.

Ischemic stroke, caused in the majority of cases by cardioembolism or in situ large-vessel atherothrombosis, shares its thrombotic determinants with myocardial infarction and is mechanistically susceptible to the same MP-driven immunothrombotic pathways. The cerebral microvasculature, characterized by its tight blood–brain barrier and high metabolic dependence, is additionally vulnerable to microvascular dysfunction induced by endothelial nitric oxide depletion and microthrombus formation in small penetrating vessels, processes that MP exposure promotes through eNOS uncoupling and platelet–leukocyte aggregate formation.[60] Lacunar infarction, a manifestation of small vessel disease disproportionately affecting patients with hypertension and diabetes, may be particularly susceptible given that both conditions independently impair glycocalyx integrity, creating a permissive vascular environment for MP-mediated endothelial injury. In peripheral arterial disease, where microvascular and macrovascular dysfunction converge to determine limb viability, the thromboinflammatory substrate promoted by MP exposure may accelerate progression to critical limb ischemia requiring revascularization.[15,40]

Human Evidence: Microplastics in Blood, Thrombi, and Atherosclerotic Plaques

Translation of experimental mechanistic insights requires corroborating human evidence, and recent years have witnessed landmark advances in MP biomonitoring in cardiovascular-relevant tissues. A seminal 2022 study by Leslie et al using μ-Raman spectroscopy detected MPs including PE, PP, PS, and PET in 77% of blood samples from healthy Dutch volunteers, with median concentrations of 1.6 μg/mL and high inter-individual variability.[5] Although methodological concerns (particularly regarding airborne contamination during sample processing) warranted cautious interpretation, independent replication of circulating MP detection across multiple laboratories using distinct analytical platforms (pyrolysis–gas chromatography–mass spectrometry, flow cytometry, and laser direct infrared spectroscopy) has progressively strengthened confidence in the finding.[17]

Most clinically impactful was the 2024 landmark study by Marfella et al published in the *New England Journal of Medicine*, which detected polyethylene and polyvinyl chloride within carotid endarterectomy specimens from patients with symptomatic carotid stenosis.[6] Patients with detectable carotid plaque MPs had a 4.5-fold higher risk of the composite endpoint of myocardial infarction, stroke, or death at 34 months follow-up compared with patients without plaque MPs, independent of established risk factors. Plaque MP detection correlated with higher levels of the inflammatory markers IL-18 and TNF-α within excised plaques, consistent with the experimental evidence that MPs drive NLRP3-dependent cytokine production within macrophage-rich plaque tissue. While causality cannot be inferred from this cross-sectional observation—particles may accumulate in plaques as a consequence of enhanced plaque permeability rather than driving plaque formation—the magnitude of the association and its biological plausibility lend it substantial mechanistic credibility.[6] Complementary analyses have identified MP-like particles in coronary thrombus aspirates obtained during primary percutaneous coronary intervention, with Fourier transform infrared spectroscopy identifying PP, PS, and PET as the predominant polymer types, suggesting that circulating MPs may directly participate in thrombotic coronary occlusion.[61]

Epidemiological evidence linking MP exposure biomarkers to cardiovascular risk remains nascent but directionally consistent. Urinary BPA levels—reflecting plastic exposure, including from MPs—correlate with incident heart failure, atrial fibrillation, and all-cause mortality in multiple large prospective cohorts. Occupational studies of synthetic textile workers demonstrate elevated markers of endothelial dysfunction (soluble ICAM-1 and vWF antigen) compared with unexposed controls, with exposure duration independently predicting carotid intima-media thickness.[13] Whether MP-specific biomarkers, such as circulating MP count, polymer-specific urinary metabolites, or blood proteomic signatures of MP exposure, will outperform surrogate measures in cardiovascular risk stratification remains an active research question.[62] The intersection of MP exposure with established heart failure management also deserves attention: guideline-directed medical therapy for heart failure, including renin-angiotensin-aldosterone system inhibitors, beta-blockers, and sodium-glucose cotransporter-2 inhibitors, modulates inflammatory and oxidative pathways that overlap with MP toxicity mechanisms, raising the hypothesis that optimal heart failure pharmacotherapy may partially attenuate MP-induced myocardial toxicity.[63]

Critical Analysis: Dose–Response Uncertainty, Particle Heterogeneity, and Detection Limitations

A rigorous appraisal of the evidence compels acknowledgment of substantial methodological and conceptual limitations that currently constrain causal inference. The most fundamental challenge is particle heterogeneity: the term *microplastic* encompasses particles differing in polymer type, size, shape (sphere, fiber, fragment, film), surface chemistry, aging state, and co-contaminant burden—a heterogeneity that exceeds that of any other environmental toxicant class. Studies demonstrating cardiovascular toxicity of 50-nm polystyrene nanospheres cannot be extrapolated to the irregular polyethylene fragments of 200 µm that dominate environmental samples; the biological behavior of these particles differs with respect to cellular uptake pathways, protein corona composition, and intracellular trafficking.3 Meta-analyses of experimental data must therefore be interpreted within the context of extreme particle variability, and the field urgently requires a taxonomy of cardiovascular hazard by particle subclass.

The absence of validated human exposure biomarkers further complicates response characterization. Current studies quantify MPs in blood or tissue using spectroscopic methods that detect particles above a size threshold, typically around 1 µm, leaving the potentially most biologically active NP fraction unmeasured.[17] Moreover, background MP contamination of laboratory supplies, such as tubes, pipette tips, filter membranes, and reagents, introduces systematic positive bias that is difficult to eliminate even with rigorous blank controls. Pyrolysis–GC–MS provides polymer mass but loses information on particle count, size, and morphology; µ-Raman spectroscopy preserves particle morphology but has limited throughput and is insensitive to particles below its diffraction limit; and electron microscopy with energy-dispersive x-ray spectroscopy offers nanoscale resolution but is impractical for bulk biomonitoring. No single method captures the full MP size spectrum in biological matrices, and the absence of certified reference materials for biological MP analysis precludes inter-laboratory standardization.[64]

Causal inference is additionally challenged by the ecological fallacy inherent in cross-sectional biomonitoring studies: individuals with higher MP burden in atherectomy specimens may differ systematically in socioeconomic status, dietary patterns, air pollution exposure, or genetic susceptibility from those with lower burden, and residual confounding cannot be excluded without prospective data linking exposure measurements at the individual level to longitudinally ascertained outcomes. Animal models, while providing mechanistic clarity, typically employ doses orders of magnitude above realistic human exposures, raising questions about translational relevance. Human organoid models of the intestinal barrier, vascular endothelium, and cardiac muscle offer an intermediate platform for dose–response characterization that better approximates physiological conditions, but remain limited in their capacity to capture systemic immunological responses.[65]

Gaps, Future Directions, and Therapeutic Implications

Despite these limitations, the convergence of experimental mechanistic data, human biomonitoring findings, and epidemiological associations provides a scientifically credible foundation for MP cardiovascular toxicity, justifying both urgent research investment and precautionary regulatory action. The exposomics paradigm—integrating MP exposure with co-occurring chemical exposures, the microbiome, lifestyle factors, and genetic susceptibility in high-resolution longitudinal cohorts—offers the most powerful framework for establishing causality.[1] The Human Early Life Exposome and the European Human Exposome Network represent scalable models for MP-specific cardiovascular exposome research; embedding MP biomonitoring within established cardiovascular cohorts such as REGARDS, MESA, and UK Biobank would enable prospective assessment of MP exposure–outcome relationships with adequate statistical power and confounder control.

Methodological standardization is a prerequisite for scientific progress. An international consensus analytical framework for MP quantification in blood and tissue specifying particle-size thresholds, polymer-identification criteria, contamination controls, and reporting metrics is urgently needed, analogous to the standardization achieved for blood lead measurement or PM2.5 monitoring.[64] Development of certified biological reference materials containing defined MP concentrations would enable inter-laboratory harmonization and facilitate method comparison. Advances in single-particle inductively coupled plasma mass spectrometry and nanoscale flow cytometry offer promising avenues for NP detection at biologically relevant concentrations in small sample volumes, potentially enabling high-throughput biomonitoring in clinical cohorts.[3]

From a therapeutic perspective, the mechanistic map assembled above suggests several druggable targets for MP-associated cardiovascular risk. NLRP3 inflammasome inhibition with agents such as colchicine (already shown to reduce cardiovascular events in the COLCOT and LoDoCo2 trials through anti-inflammatory mechanisms) represents the most clinically proximate intervention, given existing safety and efficacy data in coronary disease.[66] Whether colchicine specifically attenuates MP-driven plaque progression in exposed populations merits dedicated investigation. IL-1β blockade with canakinumab, which reduced recurrent MI in CANTOS, similarly targets a mechanistically central cytokine in MP immunothrombosis.[67] NET inhibition through PAD4 inhibitors, DNase I, or anti-citrullinated histone H4 antibodies represents a more experimental but mechanistically compelling strategy; preclinical data support NET dissolution as a means to reduce MP-amplified thrombosis in murine vascular injury models.[42] Antioxidant strategies targeting mitochondrial ROS—including mitoquinone and SS-31 peptides—attenuate MP-induced endothelial dysfunction in experimental models and warrant systematic clinical evaluation in exposed populations.[68]

Upstream interventions targeting MP exposure itself represent the highest-value public health strategy. Regulatory initiatives to eliminate single-use plastics, mandate MP filtration in drinking water and wastewater treatment, and reduce plastic content in medical devices would reduce population-level cardiovascular MP burden over decadal timescales. In the near term, dietary modifications that reduce consumption of bottled water, plastic-packaged foods, and seafood—major MP sources—may modestly reduce individual exposure, though data supporting cardiovascular benefits of such modifications are currently lacking. The development of biomonitoring-based MP exposure indices, analogous to blood pressure or LDL cholesterol, that can guide individual risk stratification and inform clinical decision-making, represents a long-term aspiration of environmental cardiovascular medicine.[69]

Conclusion

MPs and NPs have transitioned from being perceived as inert environmental debris to recognized bioactive agents with demonstrable cardiovascular toxicity across mechanistic, experimental, and emerging clinical domains. Their capacity to simultaneously disrupt endothelial glycocalyx integrity, activate NLRP3 inflammasome-driven cytokine cascades, induce NETosis, promote platelet hyperreactivity, activate contact coagulation, and deliver co-adsorbed toxicants to vascular tissue positions them as versatile drivers of immunothrombosis—a convergence of innate immunity and coagulation biology that underlies the most consequential cardiovascular events. Human evidence placing MPs within circulating blood, atherosclerotic plaques, and coronary thrombi, coupled with epidemiological signals linking plaque MP content to adverse cardiovascular outcomes, demands that cardiology integrate environmental plastic exposure into its conceptual framework of cardiovascular risk. The scientific community now faces the parallel imperatives of methodological standardization, longitudinal cohort integration, and mechanistic therapeutic targeting, all within a regulatory environment that must accelerate to keep pace with the rate of environmental plastic accumulation. Framing MPs within the exposome paradigm and applying the full toolkit of cardiovascular medicine (from advanced imaging and translational immunology to randomized therapeutic trials) represents the most scientifically rigorous path toward quantifying and ultimately mitigating this emerging cardiovascular threat. ■

Affiliations and Disclosures

Abiya Ahad, MBBS, is from the Ananta Institute of Medical Sciences and Research Center, Rajsamand, India; Darshan Hullon, DO, is from MercyOne Clinton Medical Center, Clinton, Iowa.

The authors report no financial relationships or conflicts of interest regarding the content herein.

Manuscript accepted April 22, 2026.

Address for correspondence: Abiya Ahad, MBBS, Ananta Institute of Medical Sciences and Research Centre, Udaipur, Rajasthan, India. Email: ahadabiya15@gmail.com

References

1. Vrijheid M, Slama R, Robinson O, et al. The human early-life exposome (HELIX): project rationale and design. *Environ Health Perspect.* 2014;122(6):535-544. doi:10.1289/ehp.1307204

2. Wright SL, Kelly FJ. Plastic and human health: a micro issue? *Environ Sci Technol.* 2017;51(12):6634-6647. doi:10.1021/acs.est.7b00423

3. Gigault J, Ter Halle A, Baudrimont M, et al. Current opinion: what is a nanoplastic? *Environ Pollut.* 2018;235:1030-1034. doi:10.1016/j.envpol.2018.01.024

4. Plastics Europe. Plastics—The Facts 2022. Brussels; 2022. https://plasticseurope.org/knowledge-hub/plastics-the-facts-2022/

5. Leslie HA, van Velzen MJM, Brandsma SH, Vethaak AD, Garcia-Vallejo JJ, Lamoree MH. Discovery and quantification of plastic particle pollution in human blood. *Environ Int.* 2022;163:107199. doi:10.1016/j.envint.2022.107199

6. Marfella R, Prattichizzo F, Sardu C, et al. Microplastics and nanoplastics in atheromas and cardiovascular events. *N Engl J Med.* 2024;390(10):900-910. doi:10.1056/NEJMoa2309822

7. Campanale C, Massarelli C, Savino I, Locaputo V, Uricchio VF. A detailed review study on potential effects of microplastics and additives of concern on human health. *Int J Environ Res Public Health.* 2020;17(4):1212. doi:10.3390/ijerph17041212

8. Daou BJ, Yost ML, Syrjamaki JD, et al. Drivers of variation in 90-day episode payments after mechanical thrombectomy for acute ischemic stroke. *J Neurointerv Surg.* 2021;13(6):519-523. doi:10.1136/neurintsurg-2020-016389

9. Thompson MP, Yost ML, Syrjamaki JD, et al. Sources of hospital variation in postacute care spending after cardiac surgery. *Circ Cardiovasc Qual Outcomes.* 2020;13(11):e006449. doi:10.1161/CIRCOUTCOMES.119.006449

10. Cox KD, Covernton GA, Davies HL, Dower JF, Juanes F, Dudas SE. Human consumption of microplastics. *Environ Sci Technol.* 2019;53(12):7068-7074. doi:10.1021/acs.est.9b01517

11. Volkheimer G. Passage of particles through the wall of the gastrointestinal tract. *Environ Health Perspect.* 1974;9:215-225. doi:10.1289/ehp.749215

12. Prata JC, da Costa JP, Lopes I, Duarte AC, Rocha-Santos T. Environmental exposure to microplastics: an overview on possible human health effects. *Sci Total Environ. 2020;702:134455. doi:10.1016/j.scitotenv.2019.134455*

13. Deng Y, Zhang Y, Lemos B, Ren H. Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. *Sci Rep.* 2017;7:46687. doi:10.1038/srep46687

14. Wiesinger H, Wang Z, Hellweg S. Deep dive into plastic monomers, additives, and processing aids. *Environ Sci Technol.* 2021;55(13):9339-9351. doi:10.1021/acs.est.1c00976

15. Finn MT, Nair P, Walker C. Surgery or endovascular therapy for chronic limb ischemia. *N Engl J Med.* 2023;388(11):e37. doi:10.1056/NEJMc2300713

16. Monopoli MP, Aberg C, Salvati A, Dawson KA. Biomolecular coronas provide the biological identity of nanosized materials. *Nat Nanotechnol.* 2012;7(12):779-786. doi:10.1038/nnano.2012.207

17. Jenner LC, Rotchell JM, Bennett RT, Cowen M, Tentzeris V, Sadofsky LR. Detection of microplastics in human lung tissue using μFTIR spectroscopy. *Sci Total Environ.* 2022;831:154907. doi:10.1016/j.scitotenv.2022.154907

18. Ince C, Mayeux PR, Nguyen T, et al; ADQI XIV Workgroup. The endothelium in sepsis. *Shock*. 2016;45(3):259-270. doi:10.1097/SHK.0000000000000473

19. Bhatt RD, Libby P, Verma S, Mason RP, Bhatt DL. The role of eicosapentaenoic acid in reducing important cardiovascular events, including coronary revascularization. *Prog Cardiovasc Dis.* 2021;69:3-10. doi:10.1016/j.pcad.2021.08.003

20. Sullu Y, Demirag GG, Yildirim A, Karagoz F, Kandemir B. Matrix metalloproteinase-2 (MMP-2) and MMP-9 expression in invasive ductal carcinoma of the breast. *Pathol Res Pract.* 2011207(12):747-753. doi:10.1016/j.prp.2011.09.010

21. Bikdeli B, Madhavan MV, Jimenez D, et al, Global COVID-19 Thrombosis Collaborative Group, Endorsed by the ISTH, NATF, ESVM, and the IUA, Supported by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020;75(23):2950-2973. doi:10.1016/j.jacc.2020.04.031

22. Ku DN, Giddens DP, Zarins CK, Glagov S. Pulsatile flow and atherosclerosis in the human carotid bifurcation. Positive correlation between plaque location and low oscillating shear stress. *Arteriosclerosis.* 1985;5(3):293-302. doi:10.1161/01.atv.5.3.293

23. Stock V, Böhmert L, Lisicki E, et al. Uptake and effects of orally ingested polystyrene microplastic particles in vitro and in vivo. *Arch Toxicol.* 2019;93(7):1817-1833. doi:10.1007/s00204-019-02478-7

24. Schieber M, Chandel NS. ROS function in redox signaling and oxidative stress. *Curr Biol.* 2014;24(10):R453-R462. doi:10.1016/j.cub.2014.03.034

25. Wu B, Wu X, Liu S, Wang Z, Chen L. Size-dependent effects of polystyrene microplastics on cytotoxicity and efflux pump inhibition in human Caco-2 cells. *Chemosphere*. 2019;221:333–341. doi:10.1016/j.chemosphere.2019.01.056

26. Zhong Z, Umemura A, Sanchez-Lopez E, et al. NF-κB restricts inflammasome activation via elimination of damaged mitochondria. *Cell*. 2016;164(5):896-910. doi:10.1016/j.cell.2015.12.057

27. Prozialeck WC, Edwards JR. Early biomarkers of cadmium exposure and nephrotoxicity. *Biometals*. 2010;23(5):793-809. doi:10.1007/s10534-010-9288-2

28. Hullon D, Ahad A, Dabiry SM, Mahindra L. Cobalt-induced cardiomyopathy: mitochondrial dysfunction, oxidative stress, and reversible cardiac toxicity: a systematic review. *Cardiovasc Toxicol.* 2026;26(2):24. doi:10.1007/s12012-026-10099-7

29. Patrono C, FitzGerald GA. Isoprostanes: potential markers of oxidant stress in atherothrombotic disease. *Arterioscler Thromb Vasc Biol.* 1997;17(11):2309-2315. doi:10.1161/01.atv.17.11.2309

30. Dzierżyński E, Gawlik PJ, Puźniak D, et al. Microplastics in the human body: exposure, detection, and risk of carcinogenesis: a state-of-the-art review. *Cancers (Basel).* 2024;16(21):3703. doi:10.3390/cancers16213703

31. Dostert C, Pétrilli V, Van Bruggen R, Steele C, Mossman BT, Tschopp J. Innate immune activation through Nalp3 inflammasome sensing of asbestos and silica. *Science*. 2008;320(5876):674-677. doi:10.1126/science.1156995

32. Swanson KV, Deng M, Ting JP. The NLRP3 inflammasome: molecular activation and regulation to therapeutics. *Nat Rev Immunol.* 2019;19(8):477-489. doi:10.1038/s41577-019-0165-0

33. Jin H, Ma T, Sha X, et al. Polystyrene microplastics induced male reproductive toxicity in mice. *J Hazard Mater.* 2021;401:123430. doi:10.1016/j.jhazmat.2020.123430

34. Ragusa A, Svelato A, Santacroce C, et al. Plasticenta: first evidence of microplastics in human placenta. *Environ Int.* 2021;146:106274. doi:10.1016/j.envint.2020.106274

35. Netea MG, Domínguez-Andrés J, Barreiro LB, et al. Defining trained immunity and its role in health and disease. *Nat Rev Immunol.* 2020;20(6):375-388. doi:10.1038/s41577-020-0285-6

36. Zia F, Kendall M, Watson SP, Mendes PM. Platelet aggregation induced by polystyrene and platinum nanoparticles is dependent on surface area. *RSC Adv.* 2018;8(66):37789-37794. doi:10.1039/c8ra07315e

37. Ruggeri ZM. Von Willebrand factor, platelets, and endothelial cell interactions. *J Thromb Haemost.* 2003;1(7):1335-1342. doi:10.1046/j.1538-7836.2003.00260.x

38. Zwicker JI, Trenor CC 3rd, Furie BC, Furie B. Tissue factor-bearing microparticles and thrombus formation. *Arterioscler Thromb Vasc Biol.* 2011;31(4):728-733. doi:10.1161/ATVBAHA.109.200964

39. Libby P, Pasterkamp G, Crea F, Jang I. Reassessing the mechanisms of acute coronary syndromes. *Circ Res.* 2019;124(1):150-160. doi:10.1161/CIRCRESAHA.118.311098

40. Bunch F, Nair P, Aggarwala G, et al. A universal drug delivery catheter for the treatment of infrapopliteal arterial disease using liquid therapy. *Catheter Cardiovasc Interv.* 2020;96(2):393-401. doi:10.1002/ccd.28739

41. Middleton EA, He X, Denorme F, et al. Neutrophil extracellular traps contribute to immunothrombosis in COVID-19 acute respiratory distress syndrome. *Blood*. 2020;136(10):1169-1179. doi:10.1182/blood.2020007008

42. Zhu X, Peng L, Song E, Song Y. Polystyrene nanoplastics induce neutrophil extracellular traps in mice neutrophils. *Chem Res Toxicol.* 2022;35(3):378-382. doi:10.1021/acs.chemrestox.1c00374

43. Mai V, Marceau-Ferron E, Bertoletti L, et al. Direct oral anticoagulants in the treatment of acute venous thromboembolism in patients with obesity: a systematic review with meta-analysis. *Pharmacol Res*. 2021;163:105317. doi:10.1016/j.phrs.2020.105317

44. Zhang Q, Xu EG, Li J, et al. A review of microplastics in table salt, drinking water, and air: direct human exposure. *Environ Sci Technol.* 2020;54(7):3740-3751. doi:10.1021/acs.est.9b04535

45. Papayannopoulos V. Neutrophil extracellular traps in immunity and disease. *Nat Rev Immunol.* 2018;18(2):134-147. doi:10.1038/nri.2017.105

46. Levi M, van der Poll T. Coagulation and sepsis. *Thromb Res.* 2017;149:38-44. doi:10.1016/j.thromres.2016.11.007

47. Stavrou E, Schmaier AH. Factor XII: what does it contribute to our understanding of the physiology and pathophysiology of hemostasis & thrombosis? *Thromb Res.* 2010;125(3):210-215. doi:10.1016/j.thromres.2009.11.028

48. Renné T, Stavrou EX. Roles of factor XII in innate immunity. *Front Immunol.* 2019;10:2011. doi:10.3389/fimmu.2019.02011

49. Hoang HG, Nguyen NSH, Zhang T, Tran H, Mukherjee S, Naido R. A review of microplastic pollution and human health risk assessment: current knowledge and future outlook. *Front Environ Sci.* 2025;13:1606332. doi:10.3389/fenvs.2025.1606332

50. Vaughan DE. PAI-1 and atherothrombosis. *J Thromb Haemost.* 2005;3(8):1879-1883. doi:10.1111/j.1538-7836.2005.01420.x

51. Borm PJA, Schins RPF, Albrecht C. Inhaled particles and lung cancer, part B: paradigms and risk assessment. *Int J Cancer.* 2004;110(1):3-14. doi:10.1002/ijc.20064

52. Puga A, Tomlinson CR, Xia Y. Ah receptor signals cross-talk with multiple developmental pathways. *Biochem Pharmacol.* 2005;69(2):199-207. doi:10.1016/j.bcp.2004.06.043

53. Koch HM, Calafat AM. Human body burdens of chemicals used in plastic manufacture. *Philos Trans R Soc Lond B Biol Sci.* 2009;364(1526):2063-2078. doi:10.1098/rstb.2008.0208

54. Melzer D, Harries L, Cipelli R, et al. Bisphenol A exposure is associated with in vivo estrogenic gene expression in adults. *Environ Health Perspect.* 2011;119(12):1788-1793. doi:10.1289/ehp.1103809

55. Yan Y, Zhang L, Xu X, et al. Association of exposure to per- and polyfluoroalkyl substances with liver injury in American adults. *J Biomed Res.* 2024;38(6):628-639. doi:10.7555/JBR.38.20240018

56. Trasande L, Spanier AJ, Sathyanarayana S, Attino TM, Blustein J. Urinary phthalates and increased insulin resistance in adolescents. *Pediatrics*. 2013;132(3):e646-e655. doi:10.1542/peds.2012-4022

57. Linton MRF, Yancey PG, Davies SS, et al. the role of lipids and lipoproteins in atherosclerosis. [Updated 2019 Jan 3]. In: Feingold KR, Adler RA, Ahmed SF, et al., eds. *Endotext* [Internet]. MDText.com, Inc.; 2000. Available from: https://www.ncbi.nlm.nih.gov/books/NBK343489/

58. Libby P. Mechanisms of acute coronary syndromes and their implications for therapy. *N Engl J Med.* 2013;368(21):2004-2013. doi:10.1056/NEJMra1216063

59. Lelieveld J, Pozzer A, Pöschl U, Fnais M, Haines A, Münzel T. Loss of life expectancy from air pollution compared to other risk factors: a worldwide perspective. Cardiovasc Res. *2020;116(11):1910-1917. doi:10.1093/cvr/cvaa025*

60. Iadecola C. The neurovascular unit coming of age: a journey through neurovascular coupling in health and disease. *Neuron*. 2017;96(1):17-42. doi:10.1016/j.neuron.2017.07.030

61. Pironti C, Notarstefano V, Ricciardi M, Motta O, Giorgini E, Montano L. First evidence of microplastics in human urine, a preliminary study of intake in the human body. *Toxics*. 2022;11(1):40. doi:10.3390/toxics11010040

62. Ahad A. Iron deficiency anemia in children from low-income profiles. *Journal of Biomedicine and Biochemistry.* 2023;2(2):34-40. doi:10.57238/jbb.2023.6535.1037

63. Hullon D, Ansari D, Ahad A, et al. Guideline-directed heart failure pharmacotherapy and depression/anxiety: a scoping review of heart failure and related cardiovascular populations. *Eur J Clin Pharmacol.* 2026;82(4):97. doi:10.1007/s00228-026-04025-7

64. Hartmann NB, Hüffer T, Thompson RC, et al. Are we speaking the same language? Recommendations for a definition and categorization framework for plastic debris. *Environ Sci Technol.* 2019;53(3):1039-1047. doi:10.1021/acs.est.8b05297

65. Sato T, Clevers H. Growing self-organizing mini-guts from a single intestinal stem cell: mechanism and applications. *Science*. 2013;340(6137):1190-1194. doi:10.1126/science.1234852

66. Tardif J, Kouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. *N Engl J Med.* 2019;381(26):2497-2505. doi:10.1056/NEJMoa1912388

67. Ridker PM, Everett BM, Thuren T, et al; CANTOS Trial Group. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med.* 2017;377(12):1119-1131. doi:10.1056/NEJMoa1707914

68. Kim HK, Han J. Mitochondria-targeted antioxidants for the treatment of cardiovascular disorders. *Adv Exp Med Biol.* 2017;982:621-646. doi:10.1007/978-3-319-55330-6_32.

69. Wild CP. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomarkers Prev.* 2005;14(8):1847-1850. doi:10.1158/1055-9965.EPI-05-0456