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INNO-SAFE-LIFE

Microplastics and inflammation

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Defining Microplastics

Microplastics (MPs): synthetic polymer fragments <5 mm.

Nanoplastics (NPs): <1000 nm — greater bioavailability and cellular penetration.

Primary MPs: manufactured (microbeads, fibers).

Secondary MPs: fragmentation of macroplastics via UV, mechanical, or oxidative degradation.

Common polymers: **polyethylene (PE), polypropylene (PP), polystyrene (PS), PET, PVC.**

Microplastics originate from both intentional manufacture and environmental degradation. Their small size, hydrophobicity, and chemical additives contribute to persistence and biological activity once internalized.

Sources and Environmental Distribution

Marine systems: plastic degradation, fishing gear, textile fibers.

Terrestrial sources: sewage sludge, tire wear particles, agricultural films.

Atmospheric MPs: microfibers transported via aerosols.

Human exposure routes: ingestion, inhalation, dermal contact.

MPs detected in **air, water, food, placenta, and bloodstream.**

Human exposure is continuous and multi-route. The ubiquity of MPs across environmental matrices underscores their role as chronic, low-dose immune stressors.

Physicochemical Characteristics Influencing Toxicity

Size & shape: nanoplastics cross membranes; fibers persist longer.

Surface charge: cationic MPs exhibit stronger cellular interactions.

Hydrophobicity: promotes protein corona formation.

Additives: bisphenols, phthalates, flame retardants → chemical co-toxicity.

Aging: UV oxidation introduces reactive oxygen moieties.

Physicochemical traits define the toxic potential of MPs. Nanoplastics are particularly concerning due to high surface area-to-volume ratio and potential to traverse biological barriers, including the gut epithelium and placenta.

Microplastic Uptake and Biotransport

Gastrointestinal absorption: via M-cells, paracellular transport, or Peyer's patches.

Respiratory route: alveolar macrophage uptake and translocation to lymphatics.

Cellular internalization: endocytosis, phagocytosis, or passive diffusion (NPs).

Distribution to **liver, spleen, kidney, brain, and placenta** confirmed in models.

Experimental models demonstrate systemic bioavailability. Once internalized, microplastics accumulate within lysosomal compartments, potentially initiating oxidative and inflammatory signaling cascades.

Microplastics as Inflammatory Stimuli

MPs behave as **foreign bodies** → activation of innate immune receptors.

Pattern recognition receptors (PRRs): TLR2, TLR4, NLRP3 inflammasome.

Induce **cytokine release:** IL-1β, IL-6, TNF-α, MCP-1.

Persistent exposure → chronic, low-grade inflammation (“sterile inflammation”).

Unlike pathogens, MPs trigger inflammation without infection — a process termed sterile inflammation. Their persistence sustains macrophage activation and cytokine secretion, promoting tissue remodeling and fibrosis.

Oxidative Stress and ROS Generation

Microplastic–cell interactions generate **reactive oxygen species (ROS)**.

Mechanisms: surface redox activity, mitochondrial dysfunction, NADPH oxidase activation.

Consequences: lipid peroxidation, DNA damage, ER stress.

ROS amplifies **NF-κB signaling → pro-inflammatory gene expression.**

ROS overproduction represents a key mechanistic link between MPs and inflammation. Oxidative stress is not only cytotoxic but also activates redox-sensitive transcription factors driving chronic inflammatory responses.

Inflammasome Activation

NLRP3 inflammasome activated by particle stress and lysosomal rupture.

Leads to **caspase-1 activation** → IL-1β and IL-18 maturation.

Pyroptotic cell death releases DAMPs → amplifies inflammation.

Observed in macrophages and epithelial cells exposed to polystyrene NPs.

The NLRP3 inflammasome acts as the intracellular sentinel for particulate danger. Microplastics, like silica or asbestos, disrupt lysosomal integrity, initiating inflammasome assembly and inflammatory cytokine release.

Interaction with the Immune System

Macrophage polarization: shift from M2 (anti-inflammatory) → M1 (pro-inflammatory).

Dendritic cell activation: promotes antigen presentation, Th1/Th17 differentiation.

T-cell modulation: altered cytokine milieu; decreased regulatory T-cell populations.

Systemic immune effects: chronic immune activation and tissue remodeling.

Microplastics skew immune balance toward pro-inflammatory states, enhancing systemic immune activation and lowering thresholds for autoimmune and allergic responses.

Crosstalk with the Gut Microbiome

MPs alter gut microbial diversity → **dysbiosis**.

Increased **Firmicutes/Bacteroidetes ratio** and loss of commensals.

Dysbiosis → increased **LPS translocation**, enhancing inflammation.

Gut barrier disruption (tight junction loss: occludin, claudin-1).

The gut acts as both entry and reaction site for MPs. Altered microbial ecology and intestinal permeability create a self-sustaining loop of immune activation and metabolic endotoxemia.

Systemic Inflammatory Pathways

Chronic MP exposure → systemic elevation of **CRP, IL-6, TNF-α**.

Endothelial activation → **ICAM-1, VCAM-1** expression.

Promotes **vascular inflammation** and atherogenesis.

Links observed between MPs and **metabolic syndrome** biomarkers.

Inflammation initiated in the gut or lungs can propagate systemically. Microplastics have been implicated in endothelial dysfunction, oxidative vascular injury, and chronic inflammatory conditions like atherosclerosis.

Metabolic and Cellular Consequences

Mitochondrial dysfunction: altered ATP generation and redox imbalance.

Endoplasmic reticulum stress: unfolded protein response activation.

Autophagy inhibition: accumulation of damaged organelles.

Metabolic reprogramming: Warburg-like glycolytic shift in immune cells.

Beyond inflammation, microplastics disrupt core metabolic homeostasis at the cellular level. This contributes to persistent immune activation, insulin resistance, and accelerated cellular aging.

Neuroinflammation and the Blood-Brain Barrier

Nanoplastics can cross the blood-brain barrier.

Activate **microglia** → IL-1β, TNF-α release.

Disrupt **neuronal redox balance** and synaptic integrity.

Correlated with **neurodegenerative processes** (Alzheimer's-like pathology in models).

Emerging evidence suggests neuroinflammatory potential of NPs. Chronic microglial activation may underlie cognitive dysfunctions in exposed populations, highlighting brain vulnerability to environmental particulates.

Experimental Evidence

In vitro: macrophage and epithelial cell models show cytokine release and ROS.

In vivo (mice, zebrafish): intestinal inflammation, hepatic steatosis, altered gut microbiota.

Human evidence: MPs detected in feces, blood, placenta, and breast milk.

Correlation with elevated **CRP and oxidative biomarkers** in exposed workers.

While human epidemiology is emerging, laboratory studies provide mechanistic plausibility. Animal data confirm intestinal and hepatic inflammation consistent with human biomarker trends.

Synergistic Toxicity: Additives and Adsorbed Pollutants

- MPs adsorb **heavy metals, PAHs, PCBs, pesticides**.
- Act as **vectors** enhancing bioavailability of co-contaminants.
- Combined exposure → **oxidative stress + endocrine disruption + immune activation**.
- Example: PS-NP + cadmium → synergistic hepatotoxicity.
- Microplastics amplify toxicity through “Trojan horse” effects — carrying other pollutants into biological systems. Their porous, charged surfaces concentrate hydrophobic chemicals, compounding inflammatory outcomes.

Biomarkers of Microplastic-Induced Inflammation

Cytokines: IL-6, TNF-α, IL-1β.

Oxidative markers: 8-OHdG, MDA, GSH/GSSG ratio.

Endothelial markers: ICAM-1, VCAM-1.

Transcriptomic indicators: upregulation of NF-κB, NLRP3, HSP70.

Omics approaches: proteomics and metabolomics for exposure fingerprinting.

Molecular biomarkers are critical for exposure verification. Omics-based profiling now enables identification of MP-specific inflammatory signatures in biological fluids.

Chronic Disease Associations

Metabolic disorders: insulin resistance, NAFLD, obesity.

Cardiovascular disease: endothelial inflammation, plaque formation.

Respiratory disease: chronic bronchitis, asthma exacerbation.

Cancer: chronic oxidative and inflammatory microenvironment as tumor promoter.

Persistent low-grade inflammation is a recognized precursor to chronic disease. MPs may serve as both initiators and accelerators of systemic pathologies through immune–metabolic dysregulation.

Knowledge Gaps and Research Frontiers

- Quantitative human exposure assessment lacking.
- Unknown **long-term biopersistence** of nanoplastics.
- Need for **in vivo human biomarkers** and standardized assays.
- Integrative **systems toxicology** and **multi-omics** approaches emerging.
- Ethical and policy implications of pervasive exposure.

Despite rapid advances, critical uncertainties remain in exposure quantification and risk modeling. The next frontier is linking mechanistic data with epidemiological endpoints through systems-level modeling.

Mitigation and Policy Perspectives

Source control: reduction of single-use plastics, textile filtration.

Wastewater treatment upgrades: advanced filtration, ozonation.

Human health surveillance: inclusion of MPs in environmental health monitoring.

Policy frameworks: UNEP Global Plastics Treaty, One Health integration.

Policy and technology must converge to minimize MP emissions and exposure. Integrating microplastics into One Health frameworks reflects their systemic, cross-domain impact on ecosystems and human health.

Conclusion

Microplastics act as **chronic, subclinical inflammatory triggers**.

Mechanisms: **ROS generation, inflammasome activation, immune dysregulation.**

Long-term consequences: **metabolic, cardiovascular, and neuroinflammatory diseases.**

Urgent need for **preventive policies, advanced toxicological models, and biomonitoring.**

Microplastics are more than environmental nuisances — they are biologically active particulate pollutants capable of altering immune equilibrium. Their study represents a frontier in environmental immunotoxicology.