

Microplastics in Human Blood Stream: Pathophysiological Mechanisms and Long-term Health Risks

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ABSTRACT

Background/Aim: Plastic pollution has become very widespread, which has resulted in the appearance of the problem of microplastics (MPs) as a serious ecological and health issue. According to the recent scientific discoveries, these particles are present in the bloodstream of people, which creates a challenge as to the physiological effects.

Methodology: This review will analyze the studies published within the last seven years to explain the pathways of systemic translocation, the pathophysiology of the toxicity, and the associated risks in the long-term health.

Synthesis of Literature: The indications are that MPs, mostly polyethylene, polypropylene and polystyrene, get into the circulation through ingestion and inhalation, and penetrate epithelial barriers by paracellular and transcellular means of transport. When present in the blood, they bind plasma proteins, immune cells, as well as vascular endothelium. The most important toxicological pathways are the promotion of oxidative stress, general inflammation, and procoagulant effect. In clinical practice, new longitudinal evidence relates the appearance of MPs in vascular tissue to the risk of cardiovascular diseases, both myocardial infarction and stroke.

Conclusion: This paper presents the existing issues in detection and quantification, research gaps deemed by researchers as critical and future directions of the chronic health impacts of this pre-polluted human condition.

KEYWORDS: Inflammation, Microplastic, Nanoplastic, Oxidative Stress, Pathways

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INTRODUCTION

The Anthropocene period is marked more and more by the ubiquity of synthetic polymers. Since the mid-20th century, plastic production has grown exponentially (to over 400 million tonnes per year), which has led to the extensive pollution of world ecosystems due to microplastics (MPs), which are plastic particles under 5 mm in diameter.¹ Though the first studies were mainly on marine biology and ecological effects, the introduction of MPs in the biological samples of humans, such as lungs, placentas, and feces, has changed the scientific interest to human health.² In 2022, the first conclusive study on quantifying plastic polymer in human whole blood was published and confirmed that such particles are bioavailable and circulate systemically.³

Not only does the presence of MPs in the bloodstream mark the exposure, but it is also a possible cause of systemic pathology. Since the circulatory system is the major distribution system in the body, any foreign particulate material in the body could reach any of the body organs, such as the brain, the liver and the heart.⁴ According to recent researchers, humans can consume or inhale 0.1 to 5 g of MPs per week, which is an exposure rate that highlights the importance of comprehending the biological implications of the internal dose and its effects on humans.⁵

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In the past, the medical fraternity considered plastics to be harmless materials thus making them very common in medical implants, and devices. Nevertheless, the breakdown of MPs into micro and nanoplastics (MNPs) presents another list of kinetic specifications. These particles have a high surface-area-to-volume ratio that facilitates adsorption of environmental toxin and cellular membrane interactions, which the larger materials cannot.⁶ The review is a synthesis of existing information on the way these particles enter the environment and the blood and how these particles can cause chronic disease, with a particular emphasis on the latest clinical and experimental data.

2. Pathways of Systemic Entry and Translocation

The process entails a series of steps in which the translocation of MPs into the human bloodstream involves the penetration of complicated biological

barriers. Such pathways are mainly divided into ingestion, inhalation and dermal absorption.⁶

A) Gastrointestinal Translocation and the Gut-Blood Axis

Ingestion is believed to be the most important exposure route, and the MPs get into the body through contaminated food, contaminated bottled water, and plastic wrappings.⁷ The digestive tract is engineered to receive all the nutrients but reject the pathogens and bigger particulates, but the MPs do not fit this criterion. Research has revealed that particles less than 150 µm can get across the intestinal lining, with the probability of particles less than 20 µm and NPs less than 100 nm having an even higher likelihood of getting into the lymphatic and circulatory systems.⁸

B) The major processes of translocation are:

- **Paracellular Transport:** This is the movement of particles through the tight junctions between the epithelial cells. It was found that some MPs, especially sharp-edged or jagged ones, may physically interfere with such junctions, which makes the intestinal permeability (a condition commonly called a leaky gut) more permissive and allows more systemic infiltration.⁹
- **Transcellular Transport (Endocytosis/ Phagocytosis):** Differentiated cells, e.g., M-cells in Peyer patches, have the ability to actively internalize particles and deliver them to the underlying lymphoid tissue and into the blood.¹⁰
- **Stress-resistance in the Microbiome:** MPs are able to change the composition of the gut microbiota to cause dysbiosis. The impaired microbiome also compromises the intestinal barrier, which allows entry of the plastics and the chemicals attached to plastics into the bloodstream.¹¹

C) Translocation of respiration and the Alveolar-Capillary Interface

Direct entry into the deep lung is possible through the inhalation of airborne MPs, especially synthetic fibers present in the textile/tire wear/urbust dust.¹² Particles may escape the mucociliary escalator that normally clears larger waste by passing through the blood-air barrier that is roughly 0.2 to 2.2 µm thick in the alveoli.

The smaller nanoplastics (NPs) enter the pulmonary capillaries by diffusion or alveolar macrophageal uptake. Having absorbed MPs, these macrophages can either travel through the systemic circulation or the lymphatic system, which in other words are the kind of vectors of plastic particles.¹³ This route is thus worrying, as the lungs present an open route to the left side of the heart and the systemic arterial circulation.

D) Dermal Exposure and other routes

Although the skin is a very powerful shield, according to recent research, NPs can also enter the stratum corneum, particularly when the skin is damaged or via hair follicles and sweat glands.¹⁴ Moreover, personal care items (microbeads) that contain plastic and synthetic clothes are also sources of dermal contact that exist at all times. One source of exposure that has not been considered is the direct introduction of MPs into blood through intravenous catheters or dialysis machines in clinical settings.¹⁵

3. Toxicology: Pathophysiological Mechanisms

MPs once getting into the bloodstream are considered to be non-self materials. Their level of toxicity is controlled by their physical (size, shape, surface charge) and their chemical (polymers and adsorbed additives) composition.¹⁶

A) Oxidative Stress and Mitochondrial Dysfunction

One of the major pathways of MP-induced damage is the generation of reactive oxygen species (ROS). Researchers have demonstrated that, on stimulation by MPs, membrane-bound NADPH oxidase (NOX) complexes can be activated (especially NOX2 and NOX4), and the generation of superoxide anions occurs.¹⁷ Such reactive species may disrupt mitochondrial respiration, depolarise the mitochondrial membrane and release cytochrome c, with the final result being cell apoptosis.¹⁸

Mechanical stress, which is further triggered by the inflammatory signaling pathways, can be induced by the physical friction of the irregular particles to the cellular membranes. This oxidative stress, in vascular cells, causes a decrease in the bioavailability of nitric oxide, a characteristic of endothelial dysfunction.¹⁹

B) Systemic Inflammation and Immune Response

The manipulation of the immune system by MPs is complicated. Neutrophils and macrophages tend to phagocytise circulating MPs.²⁰ The inflammasome NLRP3, which coordinates the innate immune reaction, could be activated by this process and result in the release of pro-inflammatory cytokines, including IL-1 0, IL-6, and TNF- 0.²¹

The long-term outcome of chronic exposure can be a case of long-lasting low-grade systemic inflammation. This is an inflammatory condition that is high in the levels of C-reactive protein (CRP) and other inflammatory substances in the blood. This is a known predisposing factor to a number of non-communicable diseases such as diabetes, obesity and autoimmune diseases.²² More so, MPs have been detected to disrupt the normal signaling of the white blood cells, which may inhibit the immune response to real pathogens.²³

C) Haemoglobin and Vascular Effect

- The bloodstream is a dynamic environment in which MPs are in direct contact with blood constituents. Studies have shown that there are a number of severe effects:

- **Corona Formation of the MPs:** MPs are covered instantly by the layer of plasma proteins (the corona) in the blood. This halo determines the biological identity of the particle, which affects the immune cell recognition and localization of the particle in the body. Proteins adsorbing may alter their secondary structure, which may cause protein misfolding, or they may fail to conduct their protein transport activities of oxygen and nutrients.²⁴
- **Endothelial Injury:** MPs attached to the inner (blood vessel) lining (endothelium) may cause cellular injury and denudation. This impairs vascular homeostasis and initiates monocytes recruitment, which is the initial stage of the atherosclerotic plaque development.²⁵
- **Procoagulant Activity and Thrombosis:** MPs have been observed in human thrombi (blood clots) recently. On MPs, platelet aggregation can take place, and thus they give a surface on which the coagulation cascade may be hastened. This pro-thrombotic condition comes at a very high price of exposing an individual to acute conditions such as myocardial infarction and stroke.²⁶

4. Long-term Health Risks

The chronic effects of MP bioaccumulation in blood have only recently been defined using epidemiological and clinical research.

A) The fourth disease is Cardiovascular Diseases (CVD)

The association between plastics and the heart health is no longer speculative. A groundbreaking study was published in 2024, and it was performed on patients who received a carotid endarterectomy. It determined that patients who had MPs (polyethylene and polyvinyl chloride) in the carotid plaques were at risk of getting a stroke, a heart attack, or death 4.5 times more often than those who did not have any MPs detected.²²

Presence of MPs was also linked to increased amount of the inflammatory markers in the very vascular tissue, thus indicating that the particles make the plaque to become unstable and more prone to rupture.²³ These particles might become another important non-traditional risk factor of CVD, in addition to smoking and high cholesterol, as they lead to an increase in their accumulation over decades.

B) The Blood-Brain Barrier (BBB) and neurotoxicity

As demonstrated in the experimental models, the circulating MPs can penetrate the blood-brain barrier (BBB), in particular, when the barrier is breached by old age or inflammation. By blocking the immune cells in brain capillaries following MPs in the bloodstream, MPs in the blood have been shown to cause cerebral micro-thrombosis and result in memory impairment, motor coordination impairment and anxiety-like behavior in mouse models.²⁴

Although some of these effects are acute, the neurodegenerative risks such as Alzheimer, and Parkinson

are an obvious threat in the long run. Chronic microglial activation is one of the potential causes of neural degeneration induced by the presence of foreign particles in the brain.²⁵

C) Endocrine and Reproductive disturbances

Phthalates, Bisphenol A (BPA), and per and polyfluoroalkyl substances (PFAS) are some of the many plastics that have additives that are known to disrupt the endocrine system. Whereas these chemicals may cause leaching into the bloodstream when circulating in the blood, they may directly affect the hormonal regulation when draining into the systemic circulation over a long period.²⁶

The MPs have already been found in human testicles, semen and placentas. They are theorized to be the cause of poor-quality sperm, decreasing fertility and other pregnancy complications like pre-eclampsia in the reproductive system.²⁷ Since these particles are able to bypass the placental barrier, the question of the intergenerational effect of the exposure to plastics in the future is becoming a concern and may contribute to the development of the fetus in a uterus.

D) Potential Carcinogenicity

Although the direct evidence of the connection of blood-borne MPs to cancer development in humans remains in the process of change, the clinical combination of chronic inflammation, oxidative stress, and the presence of carcinogenic additives (such as some plasticizers) gives a plausible route through which the oncogenesis process occurs. MPs can initiate tumor growth as they can provide an inflammatory microenvironment, which supports the mutation and proliferation of cells.²⁸

5. Challenges and Future Aspects

Research on MPs and its effects on human health is at a critical crossroad and is facing multiple technical and conceptual challenges.

A) Technical and Methodological Problems

It is very hard to detect MPs in blood. Background contamination is one of the most significant issues, as the plastics are ubiquitous (the materials used in the laboratory equipment, clothing, or even the air); it is necessary to make sure that the identified particles were the ones present in the blood of the patient; to achieve such a high level of accuracy, highly clean laboratories are needed.²⁸

At the moment, the quantification of polymer mass is performed by such methods as Pyrolysis-Gas Chromatography/Mass Spectrometry (Py-GC/MS), Raman microspectroscopy, and Fourier-Transform Infrared (FTIR) spectroscopy can be used to determine the type and shape of a single particle.²⁹ These techniques are however, costly and time-consuming. There is an acute necessity in the standardized and high-throughput diagnostic tools that can be utilized within the clinical pathology laboratories to test the plastic load of a patient.

A) Research Gaps: The "Real world" problem.

Majority of the extant toxicology has been in vitro work with perfectly spherical polystyrene beads of purity. These are not a true representation of irregular, weathered, and chemically complex particles in the environment.³⁰ Moreover, the research should answer the following questions:

- Dose-response Relationships: It is not yet clear what is the tipping point at which MP concentration causes clinical disease.
- The "Trojan horse Effect" MPs have the ability to adsorb heavy metals (such as lead and mercury), pesticides, and even pathogens and transfer them to the bloodstream, making them bioavailable.³¹
- Long-term Bioaccumulation: In the long term, longitudinal studies are required to establish whether the body is able to efficiently dispose such particles as time passes or whether they are stuck in the tissues decades later.

C) Policy and Mitigation

With the increasing evidence of health risks, the emphasis needs to be made on prevention. Future efforts must involve:

- Regulatory Limits: The development of safety limits of plastic particles in drinking water and food.
- Material Innovation: Innovating literally biodegradable substitutes that cannot be degraded to persistent micro-fragments.
- Clinical Guidelines: Physicians will one day be required to test patients with chronic inflammations or early cardiovascular disease, and a possible cause may be exposure to plastics.³²

DISCUSSION

The discovery of MPs in human blood is a watershed point of environmental medicine. It proves the fact that the boundary between our biological environment and the external polluted one has been violated. The circulatory system, which used to be believed to be safeguarded by a series of layers of biological filters, is currently being viewed as a pool of synthetic substances.³³

The effects of this are far reaching. Diet, sedentary lifestyles, and genetics have been identified to be the cause of the increasing number of chronic inflammation diseases over decades. Nevertheless, the fact that the number of synthetic particles in the human population is billions of particles may not be a fact that can be ignored. The MPs have also turned out to be a target of blood clots and initiator of plaque instability implying that the plaque instability is the current world epidemic of cardiovascular disease, at least in part, due to our plasticized environment.³⁴

Moreover, physical appearance of MPs in blood breaks the primary law of fluid mechanics in the blood vessels. Such

particles are able to change the blood viscosity and shear stress, causing gradual yet consistent mechanical injury on the heart and blood vessels. The overall outcome of this coupled with the chemical toxicity of the leached additives, is the so-called dual-hit model of toxicity, and until now it is not something that the human body is capable of handling.³⁵⁻³⁷ The scientific community has to shift to the next stage, that is, the phase of discovery, to the phase of mechanistic and clinical phase, to identify the ultimate causal associations and come up with the detoxification or exposure minimization strategies.

CONCLUSION

Finally, MPs are now not only an environmental problem but a serious toxicity to human health in large proportions. The studies conducted in the past 7 years prove that these particles can easily penetrate the human bloodstream via the gut and the lungs, whereby they cause pathophysiology, such as oxidative stress, chronic inflammation and vascular damage. Their presence has now been clinically associated with a higher risk of heart disease, stroke and reproductive problems.

Although the extent of the entire interaction between plastic and blood is yet to be established in detail, the survival of these materials over time is a threat to the human lifespan. The solution to this problem is also an urgent multi-disciplinary one, involving rudimentary analytical chemistry, cardiovascular medicine, and global environmental policy all in one to ensure that the human inner world does not endure irreparable damage to the inescapable effects of the plastic era.

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