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Plastic and Human Health: A Micro Issue?

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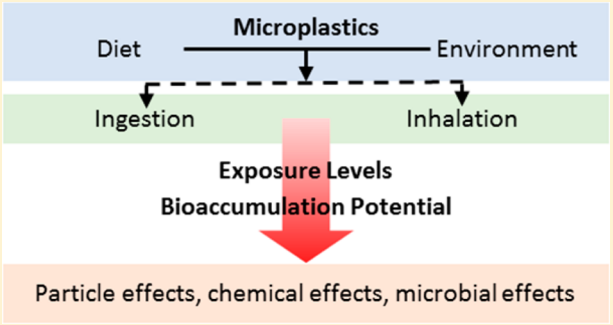
Supporting Information

ABSTRACT: Microplastics are a pollutant of environmental concern. Their presence in food destined for human consumption and in air samples has been reported. Thus, microplastic exposure via diet or inhalation could occur, the human health effects of which are unknown. The current review article draws upon cross-disciplinary scientific literature to discuss and evaluate the potential human health impacts of microplastics and outlines urgent areas for future research. Key literature up to September 2016 relating to accumulation, particle toxicity, and chemical and microbial contaminants was critically examined. Although microplastics and human health is an emerging field, complementary existing fields indicate potential particle, chemical and microbial hazards. If inhaled or ingested, microplastics may accumulate and exert localized particle toxicity by inducing or enhancing an immune response. Chemical toxicity could occur due to the localized leaching of component monomers, endogenous additives, and adsorbed environmental pollutants. Chronic exposure is anticipated to be of greater concern due to the accumulative effect that could occur. This is expected to be dose-dependent, and a robust evidence-base of exposure levels is currently lacking. Although there is potential for microplastics to impact human health, assessing current exposure levels and burdens is key. This information will guide future research into the potential mechanisms of toxicity and hence therein possible health effects.



INTRODUCTION

Plastic is a material that provides enormous societal benefit. Global production currently exceeds 320 million tonnes (Mt) per year, over 40% of which is used as single-use packaging, resulting in plastic waste.[1] A substantial proportion of the plastic produced each year is lost to and persists in the marine environment, with an estimated accumulative potential of 250 Mt by 2025.[2] Consequently, plastic debris is a critical environmental issue. Exposure to ultraviolet (UV) radiation catalyzes the photo-oxidation of plastic, causing it to become brittle. In combination with wind, wave action and abrasion, degraded plastic fragments into micro- (0.1−1000 μm)[3] and potentially nanosized (≤0.1 μm)[4] particles, referred to from herein as micro- and nanoplastics, respectively.

Microplastics are also purposefully manufactured for various applications, such as exfoliants (microbeads) in personal care products.[5] This material, along with plastic microfibers from machine-washed clothing,[6] is directly released to the environment in municipal effluent.[7] Recently, it was reported that although a wastewater treatment plant (WWTP) reduced the microplastic concentration of effluent by >98%, an estimated 65 million microplastics were still released into the receiving water daily.[8] Furthermore, in the United States, it was conservatively estimated that up to 8 trillion microbeads enter aquatic habitats each day via WWTPs, presenting a notable source.[9]

Marine debris, including glass, metals, paper, textiles, wood and rubber, is dominated by plastic. Of this, microplastics are often most common.[10] They occur in a variety of shapes; fibers are the most commonly reported form,[6] followed by fragments.[11] Microplastics are ubiquitous, having been reported in aquatic habitats worldwide from the poles[12] to the Equator.[13] An estimated 5.25 trillion plastic particles contaminate the global sea surface,[14] whereas approximately 4 billion fibers km^{-2} contaminate the deep Indian Ocean floor.[15] Even Arctic Sea ice represents a sink for microplastics, indicated by their presence in ice cores from remote locations.[16]

Nanoplastics are also increasingly being manufactured. Paints, adhesives, drug delivery vehicles, and electronics are some of the products that may contain nanoplastics.[17] 3D printing, for example, can emit polymeric nanoparticles.[18] The reduction in size, both purposefully and due to environmental degradation, may induce unique particle characteristics, which could influence their potential toxicity.

Because of their hydrophobic surface, microplastics can adsorb and concentrate hydrophobic organic contaminants (HOCs) such as polycyclic aromatic hydrocarbons (PAHs), organochlorine pesticides and polychlorinated biphenyls (PCBs) to a high degree.[19,20] They also accumulate heavy metals such as cadmium, zinc, nickel, and lead.[21,22] Microplastics are thus considered as vectors for these priority

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pollutants,[23] which are listed in the Stockholm Convention for their potential adverse health effects.[24]

Microplastics may harbor endogenous chemical additives, due to their incorporation during the manufacture of plastic products. Because these additives are not chemically bound to the plastic polymer matrix, they are susceptible to leaching to the external medium.[25] There is potential for the constant migration of intrinsic chemicals along a concentration gradient to the surface of microplastics as they continue to fragment. Such pollutants can be released upon ingestion and transfer to surrounding tissue.[26,27] If microplastics have the capacity to accumulate, they potentially present a source of chemicals to tissues and fluids, if there is any additive remaining to leach.

Emerging evidence suggests that human exposure to microplastics is plausible. Microplastics have been reported in seafood,[28−30] and in processed food and beverages such as sugar,[31] beer,[32] and salt.[33] In addition, the sludge byproducts of WWTPs that are applied to agricultural land have been found to contain synthetic (plastic) clothing fibers, which persist up to 5 years postapplication.[34] The wind-driven transport of microplastics from sludge-based fertilizer, in addition to other sources such as the degradation of agricultural polyethylene (PE) sheets or the release of fibers from drying clothes outside, could also result in airborne microplastics.[35] The atmospheric fallout of microplastics has recently been reported,[36,37] representing a possible inhalation exposure pathway. Whether microplastics and their associated chemicals are transferred to humans via diet and/or inhalation is unknown.

The quantity of microplastics in the environment is likely to increase due to the legacy of plastic items that contaminate the planet. Given the evidence suggesting human exposure to microplastics and their associated pollutants is possible, it is important to assess the risk they pose to human health. To our knowledge, there are two peer-reviewed articles that review this subject;[35,38] however, neither article considers inhalation as a potential exposure pathway, and the subsequent toxicity this could exert on the respiratory tract. We build on these two publications to incorporate the marine environment, diet, and inhalation as pathways to microplastic exposure. This review therefore aims to assess the evidence for this new potential environmental challenge by addressing the following issues: (1) dietary exposure pathways; (2) inhalation exposure pathway; (3) microplastic uptake and translocation; and (4) potential human health risks of microplastics.

EVIDENCE FOR DIETARY EXPOSURE PATHWAYS

Seafood. Given the prevalence of microplastics in the marine environment, an anticipated route of human exposure is via seafood, which forms an essential dietary component. Seafood provides almost 3 billion people worldwide with approximately 20% of their animal protein intake.[39] It is therefore one of the most important food commodities consumed globally; however, it can also be a source of environmental contaminants such as PCBs and dioxins. If seafood were to exceed regulatory levels of contaminants, there could be negative health impacts following consumption; however, these regulations are only in place for specific contaminants, e.g., mercury, not for contaminants of emerging concern such as microplastics.

Fish. Globally, fish provides approximately 4.3 billion people with 15% of their animal protein intake.[40] The capacity for fish to ingest microplastics has been demonstrated in laboratory studies,[41,42] although these employed substantially higher concentrations of microplastics than those found in nature.[43,44] Importantly, the ingestion of microplastics by fish *in situ* has been widely reported, including by commercial species, although the quantity of ingested microplastics is low (Table S1).

The occurrence of microplastics in the gastrointestinal tract (GIT) of fish does not provide direct evidence for human exposure, as this organ is usually not consumed. There is potential for the leaching and accumulation of associated chemical contaminants in edible tissue, post-microplastic ingestion. Dietary microplastic exposure via fish could be possible if microplastics were able to translocate across the GIT or gill via transcellular uptake or paracellular diffusion and enter the circulatory fluid. The respiratory epithelium of the gill is much tighter than that of mammalian lungs, decreasing the likelihood of this route of exposure; uptake across the fish gut is more likely.[45]

There is evidence for the uptake of 1 μm latex spheres from the surrounding water in rainbow trout, with particles localizing and persisting in the surface and subsurface epidermal cells of the skin and in phagocytes underlying the gill surface.[46] This highlights the importance of fish epithelial cells in the attachment and entry of microplastics. Additionally, consumption of the skin or gill tissue could present a direct route of human exposure to microplastics ($\geq$1 μm).

Shellfish. Perhaps the most important source of dietary exposure to microplastics at present is via bivalve molluscs (shellfish). Shellfish represents an important food source, comprising approximately 22 Mt of world fish production from capture and aquaculture in 2012 (almost 15 million USD).[40] Bivalves feed by pumping large volumes of water through the pallial cavity within their shells, retaining particles from suspension on their gills for subsequent ingestion.[47] Thus, they are directly exposed to microplastics via the water column. There is ample evidence for the capture and ingestion of microplastics by bivalves in laboratory studies,[48−50] and microplastics in wild and aquaculture shellfish for human consumption have been detected.

Bivalves are a popular seafood in China[28] where >60% of the global aquaculture volume is produced. This coincides with where the greatest volume of plastic enters the marine environment from land-based sources.[2] Consequently, concentrations reaching 8720 microplastics/kg of sediment, including polyethylene terephthalate (PET), polystyrene (PS) and PE particles, have been found on beaches.[51] Nine of the most commercially popular species of bivalves purchased from a fishing market in Shanghai, were found to be contaminated with microplastics (Table S2).[28] Based on the abundances observed, it was estimated that Chinese shellfish consumers could be exposed to 100 000s of microplastics each year.

The contamination of shellfish by microplastics is not limited to China. In Canada and Belgium, both wild and purchased farmed mussels were contaminated by microplastic fibers.[29,52] Farmed mussels are often cultured on deployed polypropylene (PP) lines, which may present a source of microplastics as the line degrades.[29,52] In Belgium, microplastics were recovered from farmed mussels and shop-bought Pacific oysters, which were subjected to a 3 day depuration period. Based on the average recovered concentrations, it was estimated that the average European shellfish consumer may ingest up to 11 000 microplastics per year.[30] It is of concern that following 3 days of depuration, microplastics remained in the bivalves, suggesting standard depuration periods may not be sufficient to ensure

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microplastic clearance. Shellfish food safety is an increasingly important issue with respect to microplastics.

Other Foods. In addition to seafood, potential microplastics have been reported in other foods. The presence of synthetic microfibers (minimum 40 μm in length) and fragments (mostly 10−20 μm in size) was reported in honey and sugar.[31] An average of 174 (maximum of 660) fibers and 8 (maximum of 38) fragments/kg honey, and an average of 217 (maximum of 388) fibers and 32 (maximum of 270) fragments/kg of sugar were found. Negative Rose Bengal staining determined which fibers and fragments were of synthetic origin; however, no further methods were used to identify definitively whether the particles were plastic.[31]

The contamination of honey suggests synthetic microparticles and microplastics are airborne. In support of this hypothesis, the authors reported finding 18 fibers and 4 fragments/L of rain during precipitation events. If airborne, microplastics may be deposited on flowers and foliage, where they could become incorporated with pollen and transported by bees to the hive. In support of this, the authors reported finding fibers in flowers.[31]

Perhaps even more remarkable is that the contamination of German beer by potential microplastics has been reported.[32] In all 24 samples tested, contamination by potential microplastics was found. Fragments were the most abundant, reaching up to 109 fragments/L. One suggested source was the atmospheric deposition of microplastics while a second related to the materials used in the production process.[32] Given the prevalence of microplastics in freshwater systems,[53] the water source may also be a source of contamination.

Microplastics have recently been identified in 15 brands of shop-bought sea salt. Up to 681 microplastics/kg sea salt were reported down to 45 μm. PET was the most common type of plastic found, followed by PE. It is likely that the coastal waters used to produce sea salt were the source of contamination,[33] although microplastics could also be present due to atmospheric deposition at these sites.

Clearly, microplastics currently contaminate food destined for human consumption, the impacts of which are unknown. The presence of microplastics in other foods also suggests they contaminate the atmospheric environment.

EVIDENCE FOR AN INHALATION EXPOSURE PATHWAY

In the ocean, sea salt aerosol (SSA) formation occurs due to bubbles bursting during white cap formation and wind stress, or due to waves breaking in the coastal surf zone. SSAs can range in size from <0.2 to >2000 μm diameter; the ambient mass is typically dominated by particles in the 1−10 μm range. During periods of onshore winds, they can be transported to urban environments close to the coast. Particles <50 μm are likely to have an extended atmospheric lifetime.[54] Because many plastics have a specific gravity less than seawater, it is plausible that wind action and sea spray may aerosolise sea-surface microplastics of appropriate size; however, this theory remains to be tested.

WWTP sludge byproducts applied to agricultural land have been found to contain synthetic clothing fibers, which persist in both the sludge and soil columns up to 5 years postapplication. Synthetic fibers have even been detected in field site soils 15 years after application.[34] This suggests that microplastics released via municipal effluent are retained in sludge, which is then applied as fertilizer, representing a persistent terrestrial contaminant. The wind-driven transport of microplastics from dried sludge-based fertilizer in addition to other sources such as the degradation of agricultural PE sheets[55] or the release of fibers from drying clothes[32] could all represent sources of airborne microplastics.

Recently, evidence for the presence of microplastics in atmospheric fallout has been reported.[37] The total atmospheric fallout of microplastics was assessed in a densely populated urban area and a less-dense suburban area in Paris. The majority of particles observed were fibers, approximately 30% of which were confirmed plastic. Diameters varied mainly between 7 and 15 μm and almost 25% of fibers were 100−500 μm in length; 50 μm was the limit of detection. Up to 355 particles/m^2/d were reported, with an average of 110 ± 96 particles/m^2/d. Abundances were substantially greater in urban than suburban areas.[37] Periods of heavy rainfall corresponded with some of the highest concentrations observed.[37] This preliminary study highlights the potential for human exposure to microplastics via inhalation, especially in densely populated areas.

To quantify the level of fiber exposure, a small scale study assessing 24 h personal exposure to respirable inorganic and organic fibers was undertaken at 3 European sites. Mean personal exposure levels to organic fibers (diameter <3 μm) were 0.003−0.011 fibers/mL with lengths <5 μm, 0.009−0.019 fibers/mL with lengths >5 μm, and 0.0008−0.002 fibers/mL with lengths >20 μm.[56] Although "organic" fibers (natural and manmade) included PE, PP, poly(vinyl alcohol), polyester, polyamide (PA), polytetrafluoroethylene, carbon, and natural cellulose,[56] no distinction was made regarding the composition of the fibers sampled.

Tires have recently been acknowledged as a source of microplastics. Synthetic rubber is a variation on plastic, produced by the plastics industry. It is also a hydrocarbon-based polymer, although it has different properties to plastic, such as elasticity. Tire abrasion products are a reported component of ambient particulate matter (PM). In Japan, an air sample was reported to contain 0.16 μg/m^3 of tire wear particles in the PM_{10} fraction.[57] Furthermore, the concentration of tire and road wear particles (TRWP), tire particles with road mineral incrustations, was low, with global (United States, Europe, and Japan) averages ranging from 0.05 to 0.70 mg/m^3. This comprised an average PM_{10} contribution of 0.84%.[58]

On an occupational level, indoor exposure levels can reach 0.5 and 0.8 particles/mL for polyvinyl chloride (PVC) and nylon (PA), respectively; critical particle concentrations (aspect ratio ≥3 μm) were 0.06 and 0.02/mL, respectively.[59] In the flocking area (where many small fibers are deposited onto a surface) of a flock (microfibre) manufacturing plant, the highest concentration of airborne particles reached 7 mg/m^3.[60] Polyester concentrations of 700 000 (up to 1 000 000) total fibers/m^3 and 10 000 critical fibers/m^3 were reported during processing operations.[59]

Size and exposure concentrations influence the potential risk that microplastics pose to human health. Thus, to understand the risk, it is first important to consolidate current exposure concentrations to inhalable, thoracic, and respirable particles. Airborne fibers are ubiquitous and some of these fibers are likely to be inhaled. Once they gain entry to the respiratory tract, most fibers are likely to be trapped by the lung lining fluid. However, some fibers may avoid the mucociliary clearance mechanisms of the lung, especially in individuals whose clearance mechanisms have been impaired. Occupational

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health literature specific to the synthetic textile industry provides a good indication of the anticipated hazards that microplastics, particularly fibers, may incur to human health.

MICROPLASTIC UPTAKE AND TRANSLOCATION

Fibers and Occupational Health. Studies among nylon flock workers suggest there is no evidence of increased cancer risk, although workers had a higher prevalence of respiratory irritation.[61] Interstitial lung disease, a work-related condition that induces coughing, dyspnea (breathlessness), and reduced lung capacity, has been identified in 4% of workers from nylon flock plants in the US and Canada.[62,63] Workers processing para-aramid, polyester, and PA fibers in the Netherlands presented similar symptoms, including coughing, dyspnoea, wheezing, and increased phlegm production.[64] Prick tests and nasal and inhalation provocation tests in nylon workers also found synthetic fibers, such as nylon, may act as haptens, causing an allergic reaction leading to occupational asthma.[65]

Histopathological analysis of lung biopsies from workers in the textile (nylon, polyester, polyolefin, and acrylic) industry showed interstitial fibrosis and foreign-body-containing granulomatous lesions, postulated to be acrylic, polyester, and/or nylon dust. The clinical symptoms presented were similar to allergic alveolitis (a form of inflammation in the lung).[66] Although occupational exposure likely occurs at levels higher than those in the environment, the health outcomes evidence the potential for microplastics to trigger localized biological responses, given their uptake and persistence.

Both cellulosic and plastic microfibers have been observed in non-neoplastic and malignant lung tissue taken from patients with different types of lung cancer.[67] The fibers exhibited little deterioration, supporting the notion that they are biopersistent. Additionally, these observations suggest that the human airway is of a sufficient size for plastic fibers to penetrate the deep lung; one fiber found was 135 μm in length, approximately one-quarter of the diameter of a respiratory bronchiole of generation 17 (540 μm diameter, 1410 μm length).[67] These observations confirm that some fibers avoid clearance mechanisms and, as they persist, these foreign bodies may induce acute or chronic inflammation. Importantly, rigorous sterile methods were employed throughout the sample processing in this study to prevent contamination by environmental fibers.

In addition to biopersistence, fiber dimensions play a role in toxicity. Thinner fibers are respirable, whereas longer fibers are more persistent and toxic to pulmonary cells; fibers 15−20 μm cannot be efficiently cleared from the lung by alveolar macrophages and the mucociliary escalator,[61] and fibers <0.3 μm thick and >10 μm long are most carcinogenic.[68] The use of fine-diameter (1−5 μm) plastic fibers has increased, such as in the sports clothing industry.[61] Nylon fibers of a respirable size (2 μm diameter, 14 μm length on average) interacted with the alveolar macrophages of exposed rats and were retained up to at least 29 days postexposure, causing an acute inflammatory response.[69] Shorter (9.8 μm) but wider (1.6 μm diameter) "finish-free" nylon respirable fibers, however, showed no significant impact on lung weights, pulmonary inflammation or macrophage function in male rats up to the highest concentration tested (57 fibers/cm^3) compared to control animals.[70] The burden of fibers, site of deposition and the potential for chemicals to desorb from the fiber surface also contribute to toxicity,[67] e.g., the affinity of PAHs for the hydrophobic surface of plastic[23,71] may present a route of carcinogenicity.

Potential for and Factors That May Affect Bioaccumulation. An essential factor determining whether microplastics present a physical threat or act as a vector for chemical transfer is the ability for these particles to accumulate. Throughout evolution, it is likely that both the lungs and GIT have been exposed to nondegradable, exogenous nano- and microparticles, and endogenous nanoparticles.[72,73] Consequently, the body has evolved mechanisms to respond to particle exposure (Figures 1 and 2). Recently, there has been an increased dietary influx of nondegradable microparticles, approximately 40 mg/person/day, primarily due to their inclusion as additives in processed foods.[73,74] The contribution of microplastics to exogenous microparticle exposure is unknown, however the biological response to microplastics in comparison to other nondegradable microparticles could differ due to their unique chemical composition and properties.

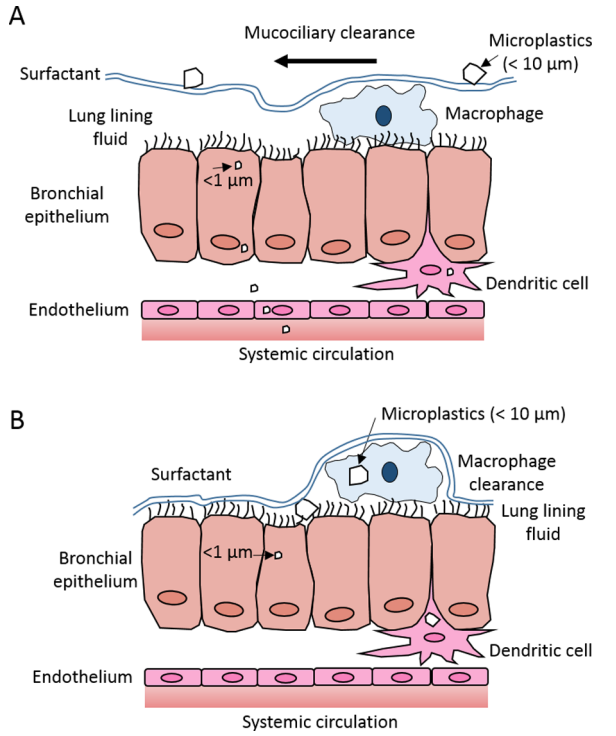

Figure 1. Potential microplastic (0.1 > 10 μm) uptake and clearance mechanisms in the lung. (A) The chance of microplastic displacement by the lung lining fluid (surfactant and mucus) is reduced in the upper airway, where the lining is thick (central lung). Here mucociliary clearance is likely for particles >1 μm. For particles <1 μm, uptake across the epithelium is possible.[107] (B) If the aerodynamic diameter of a microplastic permits deposition deeper in the lung, it may penetrate the thinner lung lining fluid and contact the epithelium, translocating via diffusion or active cellular uptake (adapted from ref 162). Reprinted from Ruge, C. A.; Kirch, J.; Lehr, C. M. Pulmonary drug delivery: From generating aerosols to overcoming biological barriers-therapeutic possibilities and technological challenges. *Lancet. Respir. Med.* 2013, 1(5), 402−413.[162] Copyright 2013 Elsevier.

Microplastics are resistant to chemical degradation *in vivo*. If inhaled or ingested, they may also resist mechanical clearance, becoming lodged or embedded. Their biopersistence is an essential factor contributing to their risk, along with dose. The uptake and toxicity of several types of polymeric nano- and

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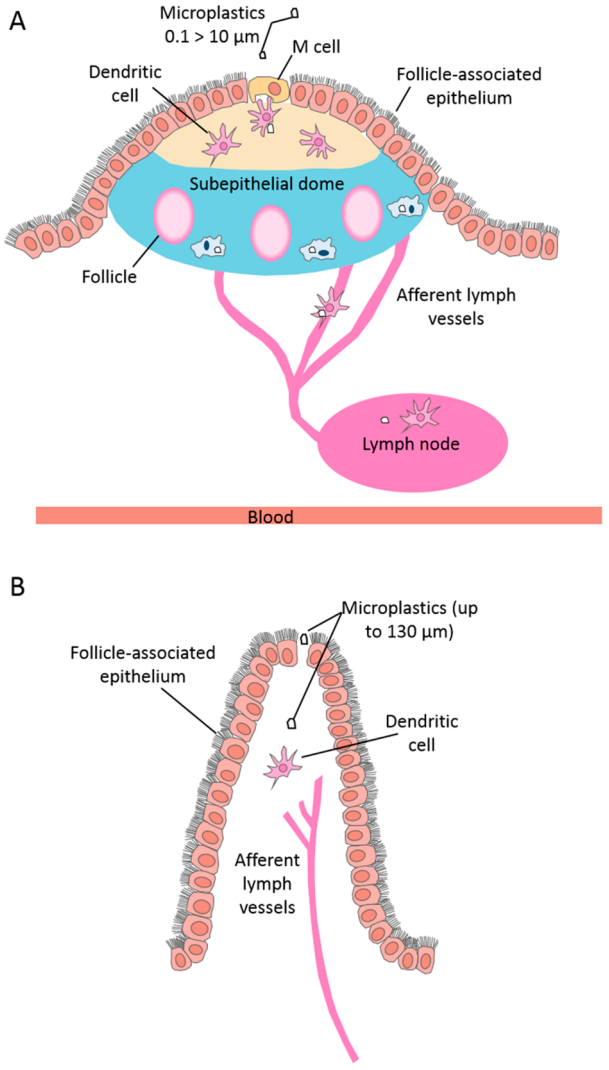

Figure 2. Predicted pathways of microplastic uptake from the gastrointestinal tract (GIT). (A) Microplastic (0.1 > 10 μm) uptake from the GIT lumen via endocytosis by the M cells of the Peyer's patches. M cells sample and transport particles from the intestinal lumen to the mucosal lymphoid tissues (adapted from ref 163). (B) Microplastic uptake from the GIT lumen via paracellular persorption. Nondegradable particles, such as microplastics, may be mechanically kneaded through loose junctions in the single-cell epithelial layer into the tissue below. Dendritic cells are able to phagocytose such particles, transporting them to the underlying lymphatic vessels and veins. Distribution to secondary tissues, including the liver, muscle and brain, could occur (adapted from ref 163). Reprinted from Mowat, A. M. I. Anatomical basis of tolerance and immunity to intestinal antigens. *Nat. Rev. Immunol.* 2003, 3 (4), 331−341.[163] Copyright 2003 Macmillan Publishers Ltd.

microparticles have been studied in model mammalian systems. The findings suggest they can translocate across living cells to the lymphatic and/or circulatory system,[72,75] potentially accumulating in secondary organs,[76−78] or impacting the immune system and health of cells.[79,80]

Retention time, and therefore the likelihood of uptake and clearance, is influenced by particle characteristics such as size, shape, solubility, and surface chemistry; by biological factors such as the anatomical site of deposition and structure; and by the nature of particle interaction with different biological structures, including the air−liquid interface, aqueous phase and free cells (e.g., macrophages, dendritic cells, epithelial cells).[81] Uptake of inhaled microplastics will depend on their wettability; it is possible that inhaled microplastics deposited on the airway will not be immersed in the lung lining fluid due to their hydrophobicity, and may therefore be subjected to mucociliary clearance leading to exposure via the gut (Figure 1). Shape also affects displacement at the air−liquid interface; shapes with sharper edges are less likely to be displaced in liquid.[82] However, the histological prevalence of plastic microfibers in flock worker[66] and lung cancer[67] tissue biopsies implies that uptake and embedment of at least plastic microfibers is possible.

As with lining fluid in the lung, mucus is the first layer in the GIT that foreign particles interact with. Here, mucus can cause particles to aggregate; surfactants reduce mucus viscosity, increasing the uptake of particles.[83] Size and surface charge also influence the ability for microplastics to cross the GIT mucus gel layer and contact the underlying epithelial cells;[84,85] smaller sizes and negative surface charge are most likely to lead to increased uptake.

If a microplastic contacts the airway or gastrointestinal epithelium, there are several routes of uptake and translocation that may occur. This is primarily via endocytic pathways in the lung and GIT, and also via persorption in the GIT (Figures 1 and 2). Paracellular transfer of nanoparticles through the tight junctions of the epithelium has been postulated for the GIT. Although tight junctions are extremely efficient at preventing such permeation, their integrity can be affected, potentially allowing for particles to pass through.[73]

Uptake Pathways. Endocytosis: Airway Surface. If an inhaled microplastic encounters the respiratory epithelium, it may translocate via diffusion, direct cellular penetration or active cellular uptake, as has been reported for other nonbiological micro- and nanoparticles.[86] The active uptake of nano- and microparticles by epithelial and endothelial cells occurs via energy-dependent endocytic and phagocytic processes.[87] Phagocytosis is the primary clearance pathway for particles 1−3 μm from the alveoli.[88] PS microparticles (1 μm) were phagocytosed by porcine pulmonary macrophages, whereas smaller PS microparticles and nanoparticles (0.2 and 0.078 μm) seemed to be passively transported via diffusion across membrane pores, as endocytic particles were not membrane-bound (Figure 1).[88]

Endocytosis: Gastrointestinal Tract. In the GIT, the Peyer's patches of the ileum (third portion of the small intestine) are considered the major sites of uptake and translocation of particles.[73,89] These domed regions are characterized by an epithelial layer of M cells, so-called due to their specialized luminal surface microfolds,[90] and enterocytes. Beneath this layer is the subepithelial dome; a cavity containing lymphocytes and/or macrophages (Figure 2A). Peyer's patches form part of the gut-associated lymphoid tissues; M cells sample and transport particles (0.1 < 10 μm) from the intestinal lumen to the mucosal lymphoid tissues,[76,91] playing a key role in immune homeostasis.[92] The subepithelial dome of the Peyer's patches act as sinks, safely storing nondegradable particles.

M cells have a high transcytic capacity.[93,94] An estimated 60% of PS nanoparticle (60 nm) uptake occurred via the Peyer's patches in rats following a 5 day oral dosing.[95] The uptake of plastic microspheres (1−2.2 μm) by the Peyer's patches has been reported in other mammalian models.[96−98] Other nondegradable microparticles, such as aluminosilicates and titanium dioxide (TiO_2), are retained in the basal phagocytes of

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the Peyer's patch, where they can occur in large numbers.[73] If microplastics also accumulate in this compartment, they could hijack the route for endogenous microparticle uptake and consequently interfere with immunosensing and surveillance, compromising local immunity.

Persorption. Another route of uptake in the GIT, and perhaps the most applicable to microplastics due to the size range it covers, is via a phenomenon known as persorption. Persorption describes the mechanical kneading of solid particles (up to 130 μm diameter) through gaps in the single-layer epithelium at the villus tips of the GIT (desquamation zones),[99] and into the circulatory system (Figure 2B).[100,101]

PVC particles (5−110 μm) have been used as model nondegradable microparticles, along with starch, to study this phenomenon.[78] Following exposure via feeding or rectal administration, the microplastics were observed to pass between enterocytes in a paracellular manner, especially in desquamation zones and between the villi. The transportation of PVC particles occurred via two routes. First by the chyle (lumen) of the underlying lymph vessels, seen in rats, guinea pigs, rabbits, chickens, dogs and pigs. Second by portal circulation, suggested by the increased occurrence of particles in blood taken from the mesenteric veins of intestinal segments of dogs fed PVC particles.[78] The appearance of PVC particles in the blood of dogs occurred rapidly postingestion; however, exposure concentrations were high −200 g of PVC powder, resulting in 10−15 PVC particles/mL of venous blood 1−2 h postingestion. PVC particles were subsequently found in bile, urine, and cerebrospinal fluid.[78] Larger particles are found in tissues and organs; PVC microparticles appeared in the liver of exposed rats, peaking 2−3 and 10 min postesophageal administration.[78] The reason for this multipeak curve has not been clarified but the study suggests that if ingested, microplastics may persorb across the intestinal wall and be transported to secondary tissues by the lymphatic and portal systems. Cerebral softening, micronecroses and scarring were observed in the brains of dogs postexposure via femoral artery catheterization into the left ventricular cavity.[100]

Persorption has been reported in human subjects. The ingestion of starch particles (200 g) led to granules being observed in urine, bile, cerebrospinal fluid, peritoneal fluid, and breast milk.[102] Particles peaked in the blood at 10 min (70 particles/10 mL) and at 110 min (90 particles/10 mL) postingestion.[102] However, the same authors found the rate (particles recovered in the blood over 24 h postexposure) of persorption to be low (0.002%).[99] Persorption is influenced by both rigidity of the particle and the level of motor activity in the GIT.[99] The rigidity of microplastics combined with a likely exposure pathway via diet suggests persorption of microplastics during the consumption of contaminated food could occur.

Factors Affecting Uptake. Following uptake, translocation can occur via macrophages to the thoracic lymph nodes, and through systemic circulation, reaching secondary target organs including the liver, kidneys, spleen, heart, and brain.[103−105] The uptake pathway largely depends on the properties of both the cell type and the target particle, including its surface chemistry and size (Figure 3).[106]

Size. Size influences the likelihood and efficiency of uptake and clearance as it governs the processes involved. Very small inhaled particles (i.e., <1 μm), or those that persist on the epithelial surface, will be taken up by cells and potentially cross the epithelium.[107] Translocation efficiency increases with decreasing size[105] and different clearance mechanisms are involved for different size fractions.[108] Based on the potential for uptake, it can be anticipated that inhaled nanoplastics would reach the deep lung and cross the lung epithelial lining, whereas microplastics may be subjected to mucociliary clearance, entering the GIT.

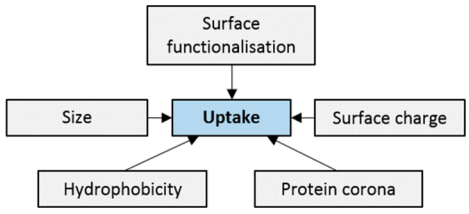

Figure 3. Particle characteristics predicted to influence micro- and nanoplastic uptake.

In the GIT, smaller particles are also postulated to translocate across the gut at a greater efficiency than larger particles; a higher abundance (34%) of 50 nm PS particles, administered (1.25 mg/kg) by gavage to rats, were taken up in comparison to larger PS nanoparticles. These smaller particles distributed to the liver, spleen, and bone marrow, whereas particles >100 nm did not reach bone marrow, and particles >300 nm were not detected in blood.[109] This contrasts to the observations of Volkheimer,[101] which suggested persorption of particles up to 130 μm across the GIT occurred. Doyle-McCullough et al.[110] reported a low uptake efficiency (0.1−0.3% of the dose) of PS microparticles (2 μm) primarily by nonlymphoid tissue, i.e., via the villi, contrasting with other studies that emphasize the role of the lymphatic Peyer's patches in the uptake of microparticles.[73,93,94]

Surface Chemistry and Hydrophobicity. Microplastic uptake and translocation will also likely be related to surface chemistry and hydrophobicity. Surface functionalization greatly influences particle recognition and uptake. Following a 2 h incubation to quartz nanoparticles with modified surfaces, most A549 human lung epithelial cells had endocytosed noncoated quartz particles whereas 15% of cells exposed to poly(2-vinylpyridine-1-oxide)-coated quartz had ingested particles.[111]

Surface charge also influences the uptake pathway. There is evidence that internalization of negatively charged PS nanoparticles is via clathrin- and dynamin-dependent endocytosis; the uptake of carboxylated PS nanoparticles by macrophages was inhibited by the presence of onodansyl cadaverine and dynasore (inhibitors of clathrin-mediated endocytosis and dynamin-dependent endocytosis, respectively). Alternatively, positively charged PS nanoparticles are internalized through micropinocytosis.[106] Surface chemistry, not charge, has been found to have a greater influence on translocation; there was a 30-fold difference in uptake between two types of negatively charged PS nanoparticles.[112]

In an *in vitro* model of human Peyer's patches, a greater proportion of PS nanoparticles (200 and 500 nm) with cationic sites were transported across than carboxylated nanoparticles. This was linked to the hydrophobicity of particles,[75] which may be attributed to better transport through the mucus layer.[81] Hydrophobicity also influences the adsorption of proteins to the particle surface, resulting in a unique protein pattern known as a corona.

Protein corona formation is strongly dependent on the chemical composition of the particle. Size is also important, as nanoparticles have a relatively large surface area per unit of mass for the adsorption of organic compounds from the

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surrounding environment.[88] It has been shown that nonbiological microparticles form biomolecule conjugates during incubation in the GIT lumen in the presence of calcium precipitates.[113] Components of the intestinal secretion, primarily endoproteins, whole and partially digested bacteria and nonabsorbed food antigens, adsorb onto the microparticle surface. Consequently, cells are exposed to conjugates of the nonbiological particle and biomolecules. Given the hydrophobic surface of microplastics, a unique assemblage of lumen components are likely to accumulate. In turn, this will encourage uptake via M-cells overlying the Peyer's patches.[113]

A factor that will affect microplastic surface chemistry is the digestive environment, where the pH changes dramatically, e.g., acidic stomach to the neutral small intestine. The action of digestive enzymes will also likely alter the chemical characteristics of microplastics as they are transported along the GIT.[73]

In addition to cellular uptake, the surface charge of microplastics may also influence the extent and pathway of translocation to secondary organs. Following an oral single dose exposure to PS nanoparticles, rats had accumulated a greater amount of negatively charged particles in almost all organs observed than positively charged particles. PS nanoparticles accumulated in the kidney, heart, stomach wall, and small intestine and the estimated bioavailability of the particles was 0.2−1.7%.[112] Despite having a low bioavailability, the PS nanoparticles still spread to secondary organs.

Elimination. Microplastics are likely resistant to degradation and will therefore persist unless eliminated. Elimination of ingested nondegradable microparticles has been observed following persoprtion across the GIT. Elimination via the bile begins several minutes postoral application, whereas elimination via urine occurs within 8 h of exposure, most of which is during the first 4 h.[101] Particles are also eliminated via urine, pulmonary alveoli, peritoneal cavity, cerebrospinal fluid, and the milk in animals and lactating women. Moreover, the passage of PVC particles via the placenta into fetal circulation has been reported.[78] This is clearly an important observation and one that deserves further investigation.

The removal of inhaled microplastics is likely to be influenced by size and surface properties. Microplastics deposited in the upper airway are likely to be cleared by mucociliary transport, and thus enter the GIT, whereas in the alveolar, macrophages are responsible for clearance.

POTENTIAL HUMAN HEALTH RISKS OF MICROPLASTICS

Potential Toxicological Pathways. Plastic is considered an inert material; however, there are pathways through which microplastics could cause harm, such as the deposition of PVC granules causing embolization of small vessels in animals following long-term oral administration.[78] Size, shape, solubility, and surface charge all influence the cytotoxicity of particles to cells and tissues *in vivo*.[114] Regarding physical effects, the biopersistence of microplastics could lead to a suite of biological responses including inflammation, genotoxicity, oxidative stress, apoptosis, and necrosis. If these conditions are sustained, a range of outcomes can ensue including tissue damage, fibrosis and carcinogenesis. Chemical effects could establish due to the composition of the polymer itself; the leaching of unbound chemicals and unreacted residual monomers; or the desorption of associated hydrophobic organic contaminants (HOCs). These are often priority pollutants with known human health effects. The cellular uptake of microplastics would allow adhered or endogenous contaminants cellular entry.[115]

Inhalation exposure studies have previously demonstrated that oxidative stress and subsequent inflammation presents the best paradigm for particle toxicity (see references within 114). Oxidative stress due to challenge with nanoparticles including PM, quartz, and TiO_2 results in airway inflammation and intestinal fibrosis.[114] A similar mechanism of toxicity may be observed for micro- and nanoplastics due to their small size and therefore large surface area for functional sites.

All plastics contain reactive oxygen species (ROS) due to their polymerization and processing history. However, the concentration of free radicals can significantly increase following interaction with light or the presence of transition metals. The weathering of plastics and microplastics leads to free radical formation by the dissociation of the C−H bonds. (see references within 116 and 117). The free radicals continue to react and therefore may pose danger. Termination of these free radical reactions is achieved through the reaction of pairs of ROS or oxidation of a target substrate, such as tissues.[116]

Inflammation and Immune Responses. *Wear Debris from Plastic Prosthetic Implants.* There is a legacy of literature concerning inflammation due to wear particles from abraded plastic prosthetic implants, which indicate the anticipatory biological reactions that may occur if microplastics were to cross the pulmonary or GIT epithelium. PE and PET wear particles have been observed in the joint capsule, cavity and surrounding tissue of patients in receipt of plastic endoprotheses. These particles range in shape from granules to spears.[118] The cellular response ranges from a few scattered cells to extensive aggregations of macrophages.[119] PE particles (0.5−50 μm) provoke a nonimmunological foreign body response.[120] Particles locate to cells,[118] and cellular aggregations resembling foreign body granulation tissue have been observed. PE particles also locate to neighboring vessels, where transportation via the perivascular lymph spaces occurs.[118] In rabbits, smaller PE particles (11 μm) were more potent than larger particles (99 μm), as indicated by a marked influx of histiocytes around the small particles.[121]

PET particles 0.5−20 μm are stored in the cytoplasm of histiocytes of the joint capsule, whereas larger particles (up to 100 μm) locate extracellularly in the tissue. The surrounding tissue changes substantially in reaction to PET particles. Joint cavities containing large quantities of fibrin exhibit necroses, and show a strong necrotic tendency and scar formation in the joint capsules. High numbers of PET particles can be phagocytosed and the granulation tissue of the joint capsule has appeared saturated, showing an incapacity to phagocytose the influx of particles and remove them to the lymph system.[118] Similar reactions to microplastics could occur if they are capable of crossing epithelia following exposure and uptake.

The removal of wear particles via proximal lymphatic channels parallels the clearance of microparticles that have crossed the GIT epithelium via persorption. In dogs, PE wear particles were found in the para-aortic lymph nodes 18 months after a total surface hip replacement.[122] In humans, PE wear particles accumulate in the lymph nodes surrounding joint replacements,[123,124] and can be so abundant that macrophages containing PE particles almost completely replace the lymph nodes.[119] PE particle-laden lymph nodes presented histiocytic infiltration (granulomatous inflammation); the histiocytes contained several PE wear particles, which induced a severe macrophage response in the surrounding tissues.[124]

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In dogs that had undergone a total surface hip replacement,[122] small deposits of PE particles were found in the alveolar walls of the lungs,[125] suggesting redistribution to secondary tissue. Additionally, in humans, PE wear particles up to 50 μm have been identified in abdominal lymph nodes. PE particles were also detected in the liver or spleen of 14% of patients.[119] The majority of particles were <1 um in size and typically accumulated in the mobile macrophages of the portal tracts of the liver, most likely by means of lymphatic transport.[119] The inflammatory response to plastic wear particles in lymph nodes has been shown to include immune activation of macrophages and associated production of cytokines.[126]

The above studies indicate the tendency for plastic microparticles to disseminate around the body, if released. Additionally, they highlight that immunological response is dependent on the chemical composition of the plastic, with PET being more harmful than PE.

Gastrointestinal Tract and Airway Surface. In the GIT, the anticipated cellular impact of microplastics will likely be due to adjuvant activity, i.e., the enhancement of an existing immune response to surface-adsorbed biomolecules.[73] When macrophages were presented with antigens and toxins conjugated to a microparticle, enhanced T cell proliferation was observed in comparison to their soluble equivalents.[127] In addition, TiO_2 nanoparticles have been shown to enhance the inflammatory response of peripheral cells to the endotoxin lipopolysaccharide. This was also enhanced in cell culture medium enriched with calcium, as the cations provide bridging potential for the adsorption of luminal proteins and present biomolecule conjugates with calcium precipitates.[113,128]

The corona, which forms on microplastics during digestive transit, could include toxins or antigens.[128,129] In addition to hydrophobicity and charge,[128] shape and age (surface pits and cracks) of the particle will impact the extent of this, as particle morphology is linked to surface area. The corona influences not just particle uptake but toxicity.[129] The topic has been widely studied from a therapeutic perspective, particularly in nano-PS.[129] However, the development of coronas on environmental microplastics is largely unstudied.

The ζ-potential (the potential difference between the particle surface and surrounding liquid media) of PS nanoparticles (193.8−344.5 nm) was associated with parameters indicative of acute pulmonary inflammation.[130] Cationic PS nanoparticles (NH_2 attachment) exhibited greater toxicity in macrophages and lung epithelial cells.[131] Surface charge has also been associated with the destabilization of membrane potential and destruction of the cellular membrane.[130] Thus, it is important to determine the surface charge and ζ-potential of environmental microplastics.

Size-related toxicity has been observed in PS nanoparticles. Smaller PS nanoparticles (64 nm) induced a significantly greater influx of neutrophils, indicative of inflammation, to the lung compared to larger nanoparticles (202 and 535 nm), following instillation in rats. This was also observed for other measures of lung inflammation. Given the low toxicity of PS, the proinflammatory effects observed were linked to the large surface area of the smaller particles.[79] Whether plastic nanoparticles also induce ROS responses in the GIT and trigger the inflammasome remains to be determined.

Chemical Transfer. *Adsorbed Chemical Pollutants.* The increased surface area:volume ratio of microplastics, combined with their surface hydrophobicity, means that a range of HOCs, including PCBs, dichlorodiphenyltrichloroethane (DDTs) and PAHs, avidly bind to their surface from the surrounding environment.[132,133] For example, concentrations of HOCs were up to 6 orders of magnitude greater on marine microplastics in comparison to surrounding seawater.[19] Recently, up to 2.4 mg/g PAHs and 0.1 mg/g DDT was reported for plastic pellets sampled from beaches in China.[134] Additionally, microplastics isolated from cosmetics were able to sorb phenanthrene and DDT from seawater,[5] highlighting the potential for primary microplastics to transfer HOCs. Some of these HOCs are highly toxic, recognized for their endocrine-disrupting, carcinogenic, mutagenic, and immunotoxic effects.

Microplastic-associated HOCs have shown to desorb to tissues in marine species upon ingestion.[26,27,135,136] Recently, the potential for HOCs to desorb from microplastics under simulated physiological conditions was studied.[137] Desorption rates in conditions simulating the digestive environment of warm blooded organisms , 38 °C, pH 4, were up to 30 times faster than in seawater.[137] Thus, in mammals including humans, the transfer of HOCs from ingested or inhaled microplastics is likely to be enhanced. This raises the question as to whether the potential uptake and biopersistence of microplastics leads to the bioaccumulation of priority HOCs and, in turn, what overall contribution this has to body burdens. Such a contribution depends on the existing concentration gradient of the HOC in question; if it is greater on the microplastics than in the surrounding environment, e.g., inside a cell or in tissue, the HOC will desorb. Although recent reviews conclude that the ingestion of microplastics is unlikely to significantly influence the exposure of organisms in the marine environment to hydrophobic organic chemicals,[138,139] the importance of this pathway in relation to others also needs addressing for humans.

Endogenous Chemical Additives. Plastic consists of a synthetic organic polymer to which chemical additives are incorporated during manufacture. These additives are included to inhibit photodegradation; to improve strength, rigidity, or flexibility; and to prevent microbial growth. Because they are not chemically bound to the plastic and are of a low molecular weight, such additives are susceptible to leaching to the external medium along a concentration gradient.[25] The continuous fragmentation of microplastics will constantly expose new surfaces, facilitating the migration of additives from the core to the surface of the particle.

If microplastics are capable of accumulating, they present a source of chemicals to tissues and fluids. This is of concern as many chemical additives and monomers have known human health effects, including reproductive toxicity (e.g., bis(2-ethylhexyl) phthalate [DEHP] and bisphenol A [BPA]), carcinogenicity (e.g., vinyl chloride and butadiene), and mutagenicity (e.g., benzene and phenol). Some of the most harmful additives include brominated flame retardants, phthalate plasticizers, and lead heat stabilizers.[140] Some plastics are combined with greater amounts of chemical additives than others, for example, PVC medical devices can contain up to 80% of the plasticizer DEHP by weight.[141] Phthalates are able to bind with molecular targets in the body, disrupting hormones.[142]

Other chemicals that could leach from the plastic polymer matrix include antioxidants, UV stabilizers, nonylphenol, and BPA.[140] The adult population is exposed to approximately 0.2−20 ng mL^{-1} BPA, with links to adverse human health effects.[143,144] The plasma concentration of BPA in adults

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exceed levels predicted from exposure via food and drink alone,[145] suggesting alternate pathways of exposure.

The ingestion and inhalation of household dust is a widely recognized human exposure pathway to flame-retarding polybrominated diphenyl ethers (PBDEs), which can reach >90 ng/g dust.[146,147] PBDEs released from plastic components, such as upholstery, carpets and electronics, lead to inhalation of ultrafine particulate PBDEs associated with dust.[148] However, the migration pathways from treated products to dust is understudied. One postulated mechanism is the transfer of PBDEs and other brominated flame retardants via the abrasion of particles and/or fibers from plastic products, i.e., microplastics. Recently, fibers and particles generated by the abrasion of brominated-flame-retardant- (BFR) treated curtain upholstery accounted for BFR concentrations in spiked ambient dust samples.[149] Thus, the accumulation of PBDEs via house dust may be due to leaching of PBDEs following the ingestion or inhalation of microplastics resulting from the wear of plastic household products and textiles.

In addition to chemical additives, plastic can also leach hazardous unreacted residual monomers. Polyurethanes, PVC, epoxy resins, and styrenic polymers have been identified as plastics of the greatest concern in terms of environmental and health effects, as their monomers are classified as carcinogenic, mutagenic, or both.[140] Currently, there is no information concerning the direct transfer of additives from plastic to human tissues, although this has been suggested for seabirds.[150] Recently, in a study investigating whether peritoneal dialysis solution (PDS) contains leached contaminants, toxic effects were observed in mice and linked to the leaching additives of the plastic PDS solution storage bags.[151]

Microbiome. In the environment, the surface of microplastics becomes rapidly colonised by microbes; well-developed biofilms establish on the surface of plastic after 7 days in water or sediment.[152,153] Such biofilms significantly differ from the ambient environment[154] and can include harmful human pathogens such as strains of Vibrio spp.[154,155]

The microbiome refers to the collection of microbial communities living on or in the body, the physiological activity of which influences host well-being.[156] It is known that the composition of the GIT microbiome can significantly differ between liquid and solid phases.[157] Thus, it can be anticipated that, in the instance that microplastics are colonised during GIT transit, the composition will differ to the surrounding environment. This is emphasized by the unique microbial assemblage that plastic attracts.[154,155] The unique coating may influence the body's response to microplastics, by enhancing bioavailability or triggering an immune response.

Environmental pollutants have shown to affect the microbiome, as microbes have the capacity to metabolize a range of environmental toxicants.[158] This can have knock on effects for the host, compromising immunity and stimulating inflammation.[156] Mice exhibited changes to the composition and function of the colonic microbiome following long-term exposure to PM_{10} administered via lavage.[159] This potentially contributed to the induction of proinflammatory cytokines in the host. However, it was unknown whether this was a direct cause of PM_{10}, PM_{10}-induced immune changes, or both.[159]

The lungs also host a microbial community that is maintained by alveolar macrophages, antibacterial surfactant, and other environmental conditions.[160] Colonisation is low in comparison to the GIT, although growth and community shifts coincide with disease.[161] Oxidative stress and inflammation have a key role in the pathogenesis of inhaled pollutants, and also modify local conditions, which potentially influence the microbiome.

Thus, the response to inhaled or ingested PM, including microplastics, may cause a shift in the microbial composition colonising the lung or GIT. Microplastics may cause inflammation or leach HOCs, the microbial metabolism of which could lead to oxidative stress. Microplastics could carry pathogenic species, or the additional substrate in the lung or GIT may facilitate growth of specific groups, shifting the assembly. Through this, alterations in the community structure and functions of the lung or GIT microbiome could occur, with knock on effects for host well-being and therefore human health.

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

Although microplastics are widely studied in the context of the marine environment where they are a prolific pollutant, we are only just recognizing the potential human exposure pathways. Following exposure, via diet and/or inhalation, uptake is plausible, as evidenced by the observations of plastic microfibers in lung tissue biopsy samples, and by the capacity for biopersistent particles up to >100 μm to cross the GIT epithelium. Following uptake, particles <2.5 μm and fibers are anticipated to be of greatest concern in the lung, whereas larger particles are of concern in the GIT due the presence of M cells

Table 1. Key Knowledge Gaps and Recommendations for Future Research into Microplastics and Human Health

Key Knowledge Gaps
What are the overall exposure concentrations from dietary and airborne sources?
What proportion of microparticle exposure do microplastic comprise?
Do different biological responses to microplastics manifest due to their unique chemical compositions/properties?
What effect does the interchangeable gastric environment/lung lining fluid have on the surface charge and chemistry, and therefore handling of microplastics?
What is the composition of the protein corona on microplastics?
Is there evidence of microplastic uptake in humans?
Are microplastics able to accumulate in the body? Do they become lodged or are they engulfed by cells?
If taken up by cells, what is the cellular mechanism of uptake? Does subcellular localization or translocation occur?
If subcellular location occurs, does this "hijack" the route for endogenous microparticle uptake or compromise immune homeostasis?
Does dissemination and/or elimination occur? Are there target secondary organs?
Are accumulative effects the same as those observed in occupational exposures?
Are larger particles a greater issue for the GIT due to the process of persorption?
What is the toxicological response to biopersistent microplastics? Do inflammatory responses mimic those observed in response to plastic prosthetics wear debris?
Do size and shape influence toxicity? Does this depend on the point of entry, e.g., are plastic microfibres of greater concern for the lung than the GIT?
Do polymer type and hydrophobicity influence toxicity?
Does surface charge of microplastics affect toxicity and does this vary with time in the environment (and therefore exposure to UV)?
Once uptaken, can microplastics deliver their chemical burden and does this cause localized toxicity?
What will the addition of the novel hard surface of microplastics, for which specific microbes and biomolecules have an affinity for, have on the microbiome?

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in the Peyer's Patches, capable of engulfing micrometer-sized particles, and the phenomenon of persorption. Toxicity is via inflammation due to the biopersistent nature of microplastics, and their unique hydrophobicity and surface chemistry. Toxicity is likely to have an accumulative effect, dependent on dose. Key knowledge gaps are outlined in Table 1.

Exposure concentrations are predicted to be low, although this is partly due to the present technical limitations in sampling and identifying microplastics. Measuring and assessing true exposure concentrations is a current scientific challenge, largely limited by particle size. Thus, current predicted exposure levels are also probably an underestimation. Once we have a better understanding of human exposure levels, and whether microplastics are uptaken/able to translocate, we can begin to unravel the potential toxicological mechanisms of microplastics and hence therein possible health effects.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.7b00423.

Occurrence of microplastics in the gastrointestinal tracts of fish *in situ*; Tables S1 and S2 (PDF)

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