The potential effects of microplastics on human health – what is known and what is unknown

Abstract

Microplastic contamination is ubiquitous in aquatic and terrestrial environments, found in water, sediments, within organisms and in the atmosphere and the biological effects on animal and plant life have been extensively investigated in recent years. There is growing evidence that humans are exposed to microplastics via ingestion of food and drink and through inhalation. Despite the prevalence of contamination, there has been limited research on the effects of microplastics on human health and most studies, to date, analyse the effects on model organisms with the likely impacts on human health being inferred by extrapolation. This review summarises the latest findings in the field with respect to the prevalence of microplastics in the human environment, to what extent they might enter and persist in the body, and what effect, if any, they are likely to have on human health. While definitive evidence linking microplastic consumption to human health is currently lacking, results from correlative studies in people exposed to high concentrations of microplastics, model animal and cell culture experiments, suggest that effects of microplastics could include provoking immune and stress responses and inducing reproductive and developmental toxicity. Further research is required to explore the potential implications of this recent contaminant in our environment in more rigorous clinical studies.

Keywords

Microplastics, human health risks, POPs, inhalation, ingestion

Introduction

Large scale production of plastics dates back to around the 1950s (Boucher and Billard 2019). In 2010, 275 million metric tons (MT) of plastic waste was generated in 192 coastal countries (Jambeck et al. 2015). By 2017 this rose to 335 million MT of plastic waste (Boucher and Billard 2019). It is also estimated that between 4.8 and 12.7 million MT of this waste enters the world's oceans (Jambeck et al. 2015). The impact of macroplastics (> 5mm in at least one dimension) through entanglement, choking and strangulation on animals has been well documented and is the more conspicuous plastic waste that is often seen in photographs depicting the scale of the plastic waste problem. Although not as obvious to the naked eye, smaller pieces of plastic debris deemed "microplastics" (MPs) (particles < 5mm in diameter but larger than 1µm (Hartmann et al. 2019) are the most abundant form of solid waste on Earth. MPs can be further categorized into primary and secondary. Primary MPs are originally made to be microsized, usually for use in cosmetic products such as microbeads (Hartmann et al. 2019). Secondary MPs refers to those that have been broken down by photo degradation or mechanical weathering over time and now fall into the <5mm definition.

MPs have been found in the ocean (Law and Thompson 2014; Auta, Emenike, and Fauziah 2017; Boucher and Friot 2017), in freshwater, (Horton et al. 2017; Vaughan, Turner, and Rose 2017; Li, Liu, and Chen 2018), in sediments (Abidli et al. 2018; Reed et al. 2018), in soils (Watteau et al. 2018; Zhang et al. 2018) and in the air (Prata 2018; Wright et al. 2020). Some of these locations are quite remote, far from human settlements. MPs have been found in remote polar regions, specifically with high concentrations seen in sea ice cores (Peeken et al. 2018). Most of the MPs detected in these ice cores were smaller than 50µm and an average of 67% of the particles were within the smallest detectable class size of 11µm (Peeken et al. 2018). They are also found in the deepest parts of the world's oceans; the

Mariana Trench sediment was found to have between 200 and 2200 pieces per litre, with the majority being plastic microfibres measuring 1-3mm in length in seawater and 0.1-0.5mm in length in sediment (Peng et al. 2018). MPs appearing in remote locations can be explained by the plastic cycle (Horton and Dixon 2018), whereby MPs accumulated in the world's oceans are so small that they can be present in the evaporation that forms our rain clouds, this rainfall containing MPs in then deposited in mountainous regions and other remote locations. The subsequent lakes and rivers transport the MPs back to the ocean, forming the plastic cycle (Geyer, Jambeck, and Law 2017; Bank and Hansson 2019). China's largest inland lake – Qinghai Lake – was found to have MPs present, with small MPs (0.1 – 0.5mm) mostly on the surface water and larger MPs (1 – 5mm) were more abundant in the connected river samples (Xiong et al. 2018). Surface water and sediment samples were collected from 6 sites along 5 different rivers in the Tibet Plateau (Jiang et al. 2019). The surface water had 483 – 967 items m^{-3} and the sediment 50 – 195 items kg^{-1}. These examples emphasise how widespread MP contamination has become.

We know that MPs are prevalent in oceans, lakes and rivers but are humans exposed to them? A review of MPs in commercial salt for human consumption found that in 128 brands of salt from 38 countries contained MPs (Peixoto et al. 2019). Similarly, MPs in bottled drinking water was found to be from the caps and could also have long-term exposure implications (Choudhary, Kurien, and Srivastava 2020). MPs have also been found in beer, energy drinks and other soft drinks (Kosuth, Mason, and Wattenberg 2018; Shruti et al. 2020) and more recently MPs (<10μm in diameter) have been found within the flesh of fruit and vegetables (Oliveri Conti et al. 2020).

There are many studies on how these MPs are ingested or inhaled and the effects this might have on wildlife (Lehner et al. 2019; Prata et al. 2020). The question is, to what extent are humans exposed and how could it affect humans? Despite the lack of knowledge about direct impacts of human health, it is acknowledged that plastic and micro plastic debris needs to be addressed (Katyal, Kong, and Villanueva 2020). Literature on the effects of MPs on other wildlife can be used as an indication of how they may impact human health and are summarised in this review. The effects of MPs on human health can be separated into three main categories; chemical, physical and biological effects and then further divided by exposure route and the potential clinical effects, as illustrated by the diagram in Figure 1.

Chemical Effects

Toxic additives

There is evidence to suggest that additives such as dyes or plasticisers could cause toxicity, carcinogenicity and mutagenicity (Gasperi et al. 2018). Additives, dyes and pigments could leach from MPs and accumulate on surfaces and in water sources, with the health consequences of this unknown (Gasperi et al. 2018).

Phthalates are commonly used as plasticizers to provide flexibility to plastics. They are an additive, therefore not chemically bound (covalently bonded) to the polymer and so are more likely to be released and transfer to the environment. Over 80% of plasticizers used worldwide are phthalates. They have been shown to appear in household dust (Abb et al. 2009; Ait Bamai, et al. 2014a), human urine (Jornet-Martínez, Antón-Soriano, and Campíns-Falcó 2015) and breastmilk (Main et al. 2006; Högberg et al. 2008). There is some evidence to suggest an association between the level of phthalates and occurrence of asthma and allergies, especially in children (Ait Bamai, et al. 2014b). Exposure to phthalates has also

been shown to have a biological effect in utero and could be associated with a shorter pregnancy duration (Latini et al. 2003). Bisphenol-A (BPA) has also been studied similarly to phthalates and shown to be a reproductive toxicant, being associated with adverse birth outcomes (Peretz et al. 2014). Monitoring of human tissues and body fluids allows us to see what concentrations of environmental contaminants are present. Biomonitoring has shown that chemicals used in the manufacture of plastics, such as BPA, phthalates and styrene, are present in the human population (Galloway 2015). Some of these chemicals have a widespread presence in the general population at concentrations capable of causing harm in animal models which raises a public health concern (Talsness et al. 2009).

Data from a study on short-tailed shearwater birds suggested that there was a transfer of plastic derived chemicals from ingested plastics to the tissues of the birds (Tanaka et al. 2013). They found brominated chemicals that were not present in the natural prey of the bird but likely from the plastic that was also found in the stomachs of some of the birds.

In a study assessing hazard levels, 31 out of 55 polymers were composed of monomers that were assigned to the most severe hazard levels (Lithner, Larsson, and Dave 2011). Polyvinyl chloride (PVC) has a carcinogenic monomer and several hazardous additives making it arguably the most dangerous plastic in terms of toxicity. An investigation into whether various plastic products emitted hazardous chemical substances into water containing *Daphnia magna* found that 9 of the 32 products caused acute toxic effects (immobility) (Lithner et al. 2009). It was also found that PVC and polyurethane leachates were the only plastic types tested that displayed toxicity.

There have been a few studies on how MPs and their additives can cause toxic effect at a cellular level, looking at cytotoxicity, oxidative stress and cell viability. Human cerebral and epithelial cells were exposed to different levels of contaminants and showed oxidative stress when MPs were introduced but there was no significant reduction in cell viability (Schirinzi et al. 2017). Another study found that the positive control induced a high degree of toxicity in all in vitro tests using direct contact (Van Tienhoven et al. 2006). An additional study found that direct contact of polypropylene MPs with human cells could induce productions of cytokines and histamines (Hwang et al. 2019).

Polybrominated diphenyl ethers (PBDEs) are additives used as flame retardants in many commercial products. Plastic can integrate up to 15% PBDEs and they are not chemically bound so are likely to leach during production, disposal and recycling processes (Domingo 2012). Concentrations of PBDEs have increased over the years in the bodies of wildlife and humans, with the long lasting effects unknown (Linares, Bellés, and Domingo 2015). There has been a handful of studies that have indicated that bioaccumulation could cause impaired neurological development (Bellés et al. 2010; Reverte, Domingo, and Colomina 2014) and endocrine disruption (Alonso et al. 2010), however, all studies were conducted on mice or rats, therefore no conclusions can be drawn on the danger to humans.

Secondary toxins

The interaction of MPs and chemical pollutants is an area widely studied (Crawford and Quinn 2017). Persistent organic pollutants (POPs) are extensively recognised to be throughout the environment, including Oceans. These pollutants are hydrophobic and have been found to readily adsorb to MPs (Velzeboer, Kwadijk, and Koelmans 2014). There are many examples of this interaction in the literature, (Rios et al. 2010; Zarfl and Matthies 2010;

149 Frias, Sobral, and Ferreira 2010; Bakir, Rowland, and Thompson 2012; Driedger et al. 2015)
150 as well as the MP interaction with heavy metals, (Ashton, Holmes, and Turner 2010; Holmes,
151 Turner, and Thompson 2012; Holmes and Thompson 2014; Rochman, Hentschel, and Teh
152 2014). For example, polyethylene mulching sheets, used in agriculture, easily fragment into
153 MPs. The longer the plastic mulching sheets are used in agriculture, the more microplastics
154 that can be found in the soil indicating that they are a major source of MPs into arable soil
155 (Huang et al. 2020a). They can also adsorb pesticides that are either in the soil or already
156 sprayed onto the plastic (Wang et al. 2020). Carbendazim, dipterex and malathion are
157 examples of the pesticides that can adsorb to MPs. It is suggested that MPs could become the
158 source or carrier of pesticides into other environments, such as water, and have the potential
159 for environmental and human safety risks. A study showed that by increasing the MP dosage
160 there was increased removal of pesticides from solution reaching equilibrium in 120 minutes
161 (Wang et al. 2020). They concluded that the adsorption was a spontaneous and exothermic
162 process. In this way, additive or sorbed chemicals including polycyclic aromatic
163 hydrocarbons (PAHs), antimicrobials, and halogenated flame retardants (HFRs) have been
164 found in laboratory studies to be transferred from MPs to marine organisms (Browne et al.
165 2013; Avio et al. 2015), however the accumulation of chemical burdens from ingested MPs is
166 not always unidirectional and depends on the concentration gradient between the ingested
167 plastics and the gut of the organism (Koelmans et al. 2016; Bakir et al. 2016). For example, if
168 an animal which already has a high concentration of chemical contamination from the
169 environment ingests microplastics with low concentrations of chemicals, the transfer is
170 expected to be from the gut to the microplastics, essentially “cleaning out” the animal.
171
172 Additionally, antibiotics can adsorb to MPs in contaminated waters and result in them being
173 transported long distances. A study found that polyamide (PA) had the highest adsorption of

antibiotics (Li, Zhang, and Zhang 2018). Five antibiotics (sulfadiazine, amoxicillin, tetracycline, ciprofloxacin and trimethoprim) and five MPs (polyethylene, polystyrene, polypropylene, PA and PVC) were investigated in both freshwater and seawater, with a higher adsorption rate of antibiotics found in freshwater compared to seawater. The same adsorption kinetics have been studied with steroid hormones, although in less depth. It has been found that 17β-estradiol and 17α-ethynylestradiol, types of synthetic hormone, will readily adsorb to MPs (Lu et al. 2020).

The potential ingestion of MPs and subsequent pollutants poses a toxic problem for the food web. Some studies have looked at how these pollutants might affect organisms (Besseling et al. 2013; Browne et al. 2013) and also look at the bioaccumulation of MPs and the pollutants (Koelmans et al. 2013). One study collected edible oysters from a coastal city in China and found MPs in all of the oyster tissue samples (Zhu et al. 2020). In addition, there was bioaccumulation of trace metals in higher concentrations than normal in the oyster tissue. It was concluded that this could pose a potential danger to humans if marine life were exposed to MPs and contaminants and then consumed.

MPs and POPs have also been found to lead to immunotoxicity in blood clams, however the larger MP size of 30μm compared to the smaller 500nm diameter appeared to mitigate the toxicity (Tang et al. 2020). On the other hand, one study concluded that the importance of MPs being a vector of toxic substances to marine organisms was of limited importance, in relation to other exposure pathways (Gouin et al. 2011). Additionally, a study on *Talitrus saltatory,* a type of amphipod, demonstrated that ingestion of contaminated MPs (polybrominated diphenyl ether) transferred organic pollutants to its tissues. However, uncontaminated MPs ingested by a contaminated amphipod removed the organic pollutants

instead (Scopetani et al. 2018). This two-way transfer could support the view that toxic substance adsorption to MPs has an equilibrium effect on marine life and is therefore a less important pathway. More research should be carried out to establish the potential of exposure to toxic pollutants carried by MPs and how they might affect human health (Rodrigues et al. 2019).

Physical Effects

Inhalation

There have been many studies that show there are MPs in the atmosphere that can be readily inhaled (Liu, et al. 2019b; Zhang et al. 2020b; Huang et al. 2020b). Production of plastic textile fibres has increased more than 6% per year and makes up around 16% of the worlds plastic production (Gasperi et al. 2018). Small fibres can shed from clothing due to general wear and washing, with just one garment predicted to release 1900 fibres per wash into waste water (Browne et al. 2011). The scale of plastic fibre production worldwide and the subsequent potential to be inhaled or ingested suggests investigations on their effects to human health should be considered.

There is research that has been conducted and is continuing to be produced, that is estimating the volume of airborne MPs across the globe. A study conducted in Central London tested atmospheric MP deposition and found it was 20 times greater than in a more remote location (Wright et al. 2020). They also found that fibrous MPs made up the vast majority of the plastics found (92%). Suspended atmospheric MPs were tested for in Shanghai, finding 0 – 4.18 m^{-3} (items per cubic meter of air) (Liu et al. 2019a). Of these 67% were microfibres, 30% fragments and 3% granules, leading to the assumption that the likely source of the majority of MPs were synthetic textiles. They also estimated that people in Shanghai inhaled

224 approximately 21 MP particles per day whilst outdoors. An earlier study of atmospheric
225 fallout in Dongguan City also found the dominant MP type to be fibres (Cai et al. 2017).
226 Similar quantities of MPs were sampled over the West Pacific Ocean, suspended in marine
227 air, with 60% microfibres, 31% fragments and 8% granules (Liu et al. 2019c). This supports
228 the conclusion that the vast majority of atmospheric MPs comes from synthetic textiles. It
229 was found that daytime collection had twice the amount as the night time collection. MPs
230 have also been found in dust in Tehran with 88-605 MP particles per 30g of dry dust
231 (Dehghani, Moore, and Akhbarizadeh 2017). They also estimate that outdoor activity can
232 lead to an estimated exposure of 3223 particles per year for children and 1063 particles per
233 year for adults. A similar study in Iran found on average 900 MP particles in 15g of street
234 dust (Abbasi et al. 2019).
235
236 Atmospheric MPs can also be sourced from deposition, or rain. A study in Paris detected
237 MPs in atmospheric fallout, with the results finding 29 – 280 particles m^{-2} day^{-1} (Dris et al.
238 2015). Atmospheric deposition has also been tested in remote environments (Zhang et al.
239 2019). One study found 249 fragments, 73 films and 44 fibres per square meter in the
240 catchment area of the French Pyrenees (Allen et al. 2019). They concluded that the MPs
241 could travel up to 95km to reach more remote areas via atmospheric transport. A similar
242 study instead looked at a glacier in the Italian Alps and found 74.4 MP items kg^{-1} of sediment
243 (Ambrosini et al. 2019). This contained most commonly polyesters, but also polyamide,
244 polyethylene and polypropylene. Furthermore, they estimate that the whole glacier could
245 have 131-162 million plastic items.
246
247 The effects on human health of inhaling these fibrous MPs is little understood. It is thought
248 that the majority of fibres can be cleared from the respiratory system, however some will go

on to cause inflammatory responses and even respiratory lesions (Prata 2018), especially in those with compromised clearance mechanisms (Gasperi et al. 2018). Of 114 lung specimens from patients undergoing lung resection for removal of a tumour, 87% were observed to contain cellulosic or plastic fibres, demonstrating that these small fibres are respirable and accumulate in lung tissue (Pauly et al. 1998). Synthetic textiles are thought to be the main source of airborne MPs, especially indoors where the concentration is greater (Dris et al. 2017). It has been studied previously that inhalation of fibres during factory work can cause some cancers (Gallagher et al. 2015), however some studies on nylon flock workers suggested that there was no evidence of an increased cancer risk, but there was a higher prevalence of respiratory irritation (Wright and Kelly 2017).

We know that the lungs are exposed daily to pollutants which act as oxidants and this leads to oxidative stress, inflammation and carcinogenesis (Valavanidis et al. 2013). There is also an association between the increased incidence of respiratory disease and lung cancers from the exposure to low levels of respirable fibres (Valavanidis et al. 2013). However, little research has been conducted on the potential adverse health effects on human lungs when inhaling synthetic fibres and is therefore difficult to attribute this increase in respiratory disease to inhaled MPs (Gasperi et al. 2018). A study investigating proinflammatory responses in rats to various sizes of polystyrene particles found that the smaller particles (64nm) gave a significantly greater neutrophil influx in the lungs compared to the larger particles (202nm – 535nm) (Brown et al. 2001). It is thought that this is due to the larger surface area of smaller particles, leading to increased inflammation. There is evidence to suggest that MPs could also translocate to other tissues once inhaled or ingested, with one study finding that fluorescent polystyrene microspheres delivered intranasally to mice could be found in the spleen 10 days later (Eyles et al. 2001). It was also found that once there, they could incite immunological

functions. There is little to no information available on any human studies looking at health effects of MP fibre or particle inhalation, something that should be investigated in the future.

Ingestion

A considerable amount of MP research is conducted on ingestion by aquatic life, (Possatto et al. 2011; Lusher, McHugh, and Thompson 2013; Phillips and Bonner 2015; Romeo et al. 2015; Barboza et al. 2018) on seabirds, (van Franeker et al. 2011; Lavers, Bond, and Hutton 2014; Amélineau et al. 2016) and other wildlife (Huerta Lwanga et al. 2016), with limited studies conducted on human ingestion (Ribeiro et al. 2019). One study compared human ingestion of MPs from mussels with the inhalation of microfibres whilst eating that same meal and found that you inhale more synthetic microfibres sitting down for a meal than you would from eating the mussels (Catarino et al. 2018). There is however, some proof that humans ingest MPs, when one study tested 8 human stool samples and found MPs in all of them (Schwabl et al. 2019). They found that polypropylene and polyethylene terephthalate were the most abundant types of plastic. It is also known that MPs are present in seafood (Li et al. 2016), water, salt and beer (Kosuth, Mason, and Wattenberg 2018) and in potentially more food or drink items that are regularly consumed by humans (Zhang et al. 2020a).

An evaluation of the number of MPs consumed from the average intake of food found that the average annual consumption was in the range of 39 000 – 52 000 particles (Cox et al. 2019). This could increase to between 74 000 – 121 000 when the inhalation of MPs was considered. They also found that if you included water intake from only a bottle source then an individual could be ingesting a further 90 000 particles compared to 40 000 particles consumed from tap water. Edible fruits and vegetables provide further example of the potential ingestion of MPs by humans. A study found that apples were the fruit most

299 contaminated with a median of 223 000 p/g of MPs. It was further calculated that the
300 estimated daily intake of MPs from apples was 4.62 E+05 for adults and 1.41E+05 for
301 children (Oliveri Conti et al. 2020).
302
303 One study in China comparing MPs in fish and bivalves in cities with other countries in the
304 world, found that MPs are prevalent in commercial fish and bivalves sold in city markets and
305 that the risk to human health is greater from these markets than other countries in the world
306 (Fang et al. 2019). A more recent study looked at 150 fish from 3 species and found 49% had
307 MPs, of this 32% was found in the dorsal muscle of the fish with a mean number of 0.054
308 items per gram (Barboza et al. 2020). Based on the fish muscle data and the recommended
309 human consumption of fish per capita in selected European and American countries,
310 researchers were able to estimate that adults potentially consume 518 – 3078 MP
311 items/year/capita. These numbers are considerably smaller than the 39 000 mentioned earlier,
312 however the figure was based on data from one type of fish; consumption of other products
313 containing MPs were not considered.
314
315 Although most studies look at non-human MP ingestion, they can be used to look at the
316 effects this might have on tissues and organs. A study on tissue accumulation of polystyrene
317 in zebrafish found 5μm diameter MPs in the gills, liver and gut and 20μm diameter
318 accumulation in just the gills and gut. This caused inflammation and lipid accumulation.
319 They also found that exposure to MPs induced alterations of metabolic profiles in the liver
320 and disturbed lipid and energy metabolism (Lu et al. 2016).
321
322 In a separate study, Zebrafish were exposed to three shapes of MPs (bead, fragment and
323 fibre). There was accumulation of the MPs in the gut, with the fibre shape resulting in the

more severe intestinal toxicity than fragments and beads. The accumulation caused mucosal damage, increased permeability, inflammation, metabolism disruption and microbiota dysbiosis (Qiao et al. 2019). A different study found that fish with MPs had significantly higher lipid peroxidation levels in the brain, gills and dorsal muscle and increased brain acetylcholinesterase activity than fish with no MPs, suggesting lipid oxidative damage (Barboza et al. 2020). Medaka fish larvae and juveniles were fed food spiked with environmental MPs in a different study. They found that in those fed the spiked food it could cause death, decreased head/body ratios, increased Ethoxyresorufin-O-deethylase (EROD) activity, DNA breaks and alterations to swimming behaviour (Pannetier et al. 2020).

There was also a study that looked at polystyrene MPs in mice based on toxicity-based toxicokinetic/toxicodynamic modelling to quantify organ bioaccumulation and biomarker responses. The gut had the highest bioaccumulation factor and overall the smaller MP size (5μm) exhibited higher values compared to the larger MP size (20μm) (Yang et al. 2019b). Another study on mice and polystyrene MPs looked at tissue distribution, accumulation and tissue-specific health risks. They were found to accumulate in the liver, kidneys and gut, depending on particle size. Biochemical biomarkers suggested exposure induced disturbance of energy and lipid metabolism as well as oxidative stress (Deng et al. 2017). There is however, an editorial that is critical of this Deng et al. study, suggesting that the conclusion of health effects by MPs is not sufficiently supported by the data presented (Braeuning 2019). They also question the values given for the accumulation of plastic in organs as the figures seem to far exceed the doses administered.

A different study looked at the exposure to differing amounts of polyethylene MPs in mice. The high concentration of MPs increased the numbers of gut microbial species, bacterial

abundance and flora diversity. Serum levels of interleukin 1a in all feeding groups were significantly greater than in the blank group. The intestines of mice fed high concentrations of MPs showed inflammation and higher TLR4, AP-1 and IRF5 expression (Li et al. 2020). A contrasting study looked at the intestinal particle uptake and health-related effects of oral polystyrene in vitro and in vivo. It suggested that oral exposure to polystyrene in the conditions tested did not pose any relevant acute health risks to mammals; no inflammatory response or lesions and no interference of macrophages (Stock et al. 2019).

There should also be consideration for the effects of MPs on offspring during gestation. In a recent study, pregnant mice were exposed to polystyrene MPs in their drinking water and the offspring observed and tested. They found that there was no significant effect on the offspring's growth, however there was indication of the offspring having fatty acid metabolic disorders, which was related to the MP particle size (Luo et al. 2019). Another study used an ex vivo human placental perfusion model and fluorescently labelled polystyrene beads from 50nm – 500nm in diameter to see if the particles could cross the placental barrier and affect the foetus (Wick et al. 2010). They found that a diameter of up to 240nm was able to cross the placental barrier but did not affect the viability of the placental explant.

As mentioned previously there is a wide occurrence and reporting of MP ingestion by aquatic fauna but there are questions as to how much of this actually transfers to humans in terms of ingestion. Most studies that look at the health effects are produced in laboratory conditions which are less relevant when applied to the environment. In particular there is a need to be realistic with the concentrations of MPs used and aligning them with what would most likely be found in the environment (de Sá et al. 2018; Wang et al. 2019).

Prosthetics

There has been limited studies on MPs generated by wear and corrosion of joint replacement prostheses, however one published in 2000, details identification of metallic and polyethylene particles from post-mortems in 29 patients (Urban et al. 2000). They found polyethylene particles in the para-aortic lymph nodes in 68% of 28 patients and in the liver or spleen of 14% of 29 patients. The majority of the particles were less than 1μm in size and mostly in low concentrations, with little pathological importance. However, in one case granulomas formed in the liver, spleen and abdominal lymph nodes in response to heavy accumulation of wear debris from a hip prosthesis. Additional studies related to plastic prosthesis particle contamination have been carried out in vitro or using in vivo models and seek to explore the health effects of the wear debris. An in vitro study found that when adding polymethylmethacrylate (PMMA) particles to each developmental stage of osteoclasts there was an increase in bone resorption in mature osteoclasts (H. Zhang et al. 2008). It is thought that inflammation is caused by PMMA particles increasing osteoclast formation resulting in prosthetic failure. Similarly, ultra-high molecular weight polyethylene (UHMWPE) particles were introduced to bone implants in mice and then treated with erythromycin 2 weeks after implantation (Markel et al. 2009). Results showed that exposure to UHMWPE particles induced inflammation and increased bone resorption, but with erythromycin treatment, this was reduced. A study in 2011 looked at toll-like receptors (TLRs) and their role in recognising orthopaedic implant wear-debris particles, ultimately causing inflammation (Pearl et al. 2011). They found that TLRs signal through myeloid differentiation factor 88 (MyD88) and by inhibiting MyD88 there was a decrease in PMMA particle induced production of macrophages and therefore, inflammation.

Biological effects

Microorganisms

It has been shown that bacteria can rapidly colonize MP surfaces in the marine environment (Harrison et al. 2014; Wagner et al. 2014), as well as form microbial biofilms (Lobelle and Cunliffe 2011). Zettler et al. studied plastic marine debris using a scanning electron microscope (SEM) and found a diverse microbial community coined a 'Plastisphere' (Zettler, Mincer, and Amaral-Zettler 2013). They found that the hydrophobic surface of these plastics is ideal for microbial colonization and biofilm formation, discovering that the most abundant genus was *Vibrio,* among many others. Although there is sufficient research showing that microorganisms can colonise MPs, there is little evidence of whether or not they are capable of degrading MPs in the field. Laboratory studies, however, indicate that fungi, bacteria and biofilms are capable of degrading MPs of a variety of polymer types including polyethylene, polystyrene and polylactic acid (Yuan et al. 2020).

Potentially pathogenic *Vibrio* spp. were found to be present on floating MPs in water samples from the North and Baltic Sea, which suggests MPs could function as vectors for the dispersal of pathogens (Kirstein et al. 2016). The *Vibrio* spp. Pathogen could cause serious infections in humans if ingested (Morris Jr. and Acheson 2003), illustrating that the presence of MPs in seafood is an area to be investigated further.

There is some evidence to suggest that interactions between MPs, microorganisms and gut microbiota could lead to health implications (Lu et al. 2019). It is known that gut microbiota plays an important role in the hosts health and it is also known that MPs can carry potential pesticides, fungicides and pathogens. Once ingested these hitchhikers may affect health by changing the composition of gut microbiota (Lu et al. 2019).

A further area of interest is the antibiotic resistant bacteria (ARB) that has been found on some MPs (Yang et al. 2019a). A recent study found ARB counts on MPs were 100 – 500 times higher than those in water and the ratios of ARB to total bacteria from MPs were higher than those in water (Zhang et al. 2020c). They also looked at multi-antibiotic resistant bacteria (MARB) and found penicillin, sulfafurazole, erythromycin and tetracycline resistant bacteria, accounted for 25.4% on MPs compared with 23.9% in water. Further studies looking at antibiotic resistant genes (ARG) showed a detection rate up to 80% on MPs and 65% in water (Zhang et al. 2020c). It was concluded that MPs can provide a beneficial surface for ARB to form a biofilm and facilitate horizontal gene transfer, which they would otherwise be unable to do in water alone and this could lead to the enrichment of superbugs.

Conclusion

There is a growing body of literature demonstrating that the atmosphere and human food and water sources are contaminated by MPs and may, therefore, be inhaled or ingested by humans. Studies using model organisms indicate that ingestion of microplastics might cause harm to organisms via their physical presence (abrasive effects leading to inflammation, oxidative stress and cytotoxicity), their chemical burden (leaching of additives or adsorbed chemicals from the environment causing reproductive and developmental toxicity or invoking an immune response) or their microbial communities (pathogens causing infection, gut dysbiosis or antimicrobial resistant microbes entering the body). In addition, inhalation of plastic microfibres has become a key research focus with recent estimates suggesting the general population inhales hundreds of plastic fibres each day. Correlative research links inhalation of plastic fibres to respiratory disease, inflammation and oxidative stress making inhalation of microfibres a key area of concern given the growing dominance of synthetic

fibres in the clothing industry. The actual concentrations of inhaled and ingested microplastics that are accumulated within the human body are, however, not yet known. There is still a dearth of data on the direct human health implications and future work should target the direct effects of MPs on human health by focusing on inflammation and cellular damage at concentrations realistically reflecting environmental exposure.

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Figure 1

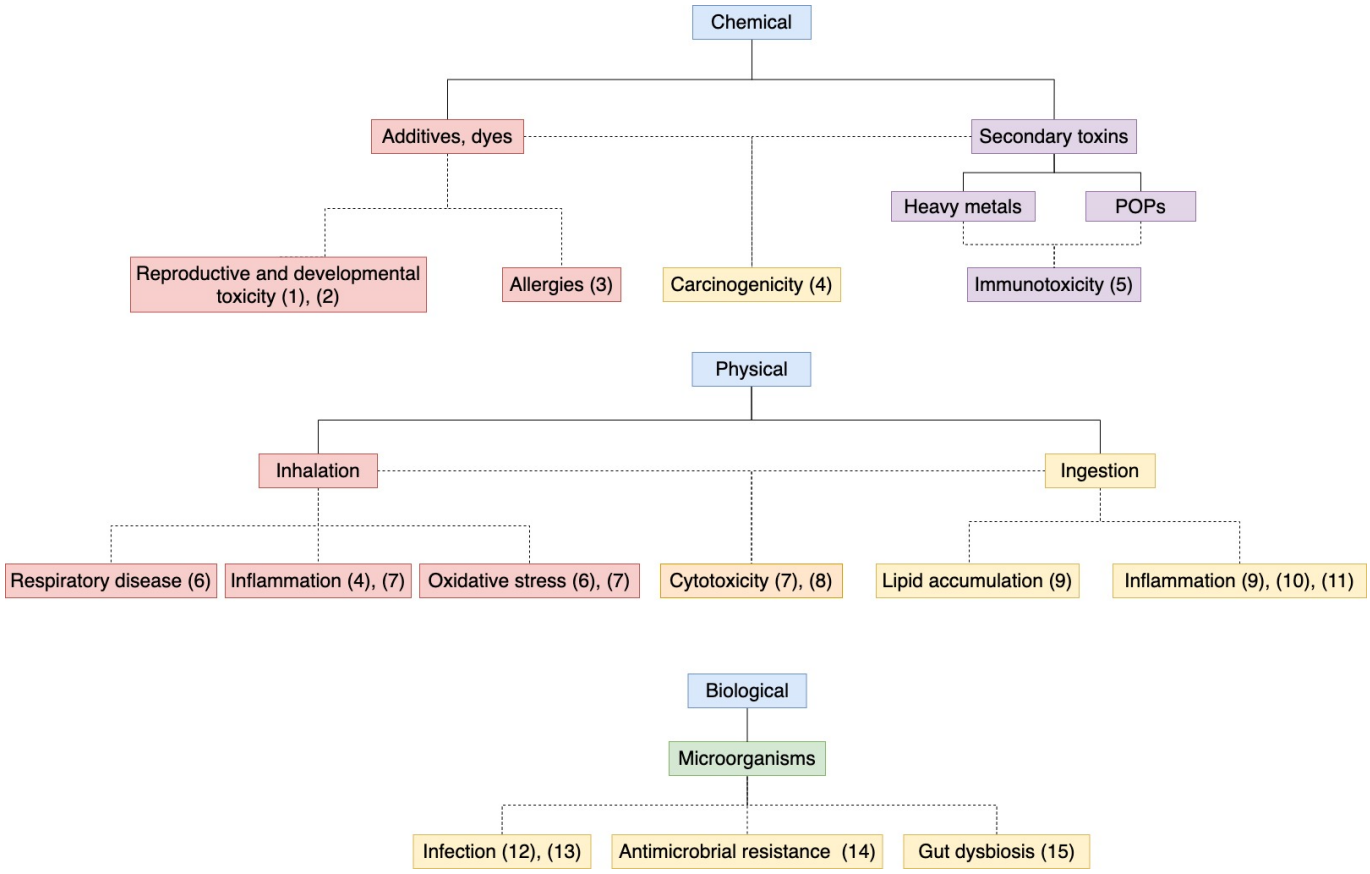

Figure 1 - Flow diagram to illustrate the potential human health effects of microplastics. Dotted lines represent current speculative research. (1) Giuseppe et al. 2003, (2) Peretz et al. 2014, (3) Ait Bamai et al. 2014b, (4) Gasperi et al. 2018 (5) Tang et al. 2020, (6) Valavanidis et al. 2013, (7) Prata 2018, (8) Gallagher et al. 2015, (9) Lu et al. 2016, (10) Qiao et al. 2019, (11) Li et al. 2020, (12) Morris and Acheson 2003, (13) Kirstein et al. 2016, (14) Yang et al. 2019a, (15) Lu et al. 2019.