

The Potential for Human Health Effects from Microplastics

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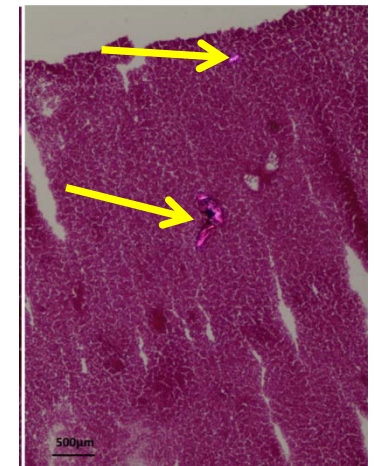
March 28, 2019

Outline

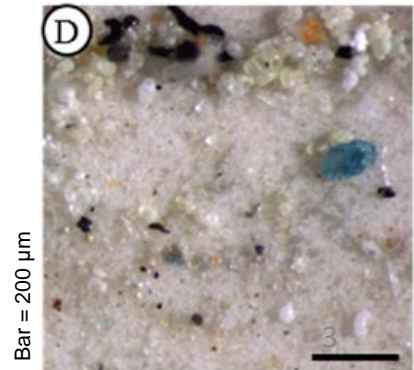
- *Are microplastics a risk to human health?*
- Sources of human **exposure**
- Health **hazards** of microplastics
- Government reports
- Potential research

Sources of Human Exposure

- Consumption of contaminated foods and beverages
 - **Bivalves**
 - Found in farm-raised mussels and oysters
 - **Finfish**
 - Found in gastrointestinal tracts
 - Possibility for translocation across the gut, into circulation, and embedded into edible tissue
 - Lab experiments demonstrate microplastics in liver
 - **Table salt**
 - Harvested from the sea, lakes, or wells
 - **Beverages**
 - Bottled water
 - Tap water
 - Beer
- **Issues with source of microplastics**
 - Laboratory contamination (airborne microfibers)
 - Processing or packaging of consumables
 - Plumbing



Bar = 500 μm



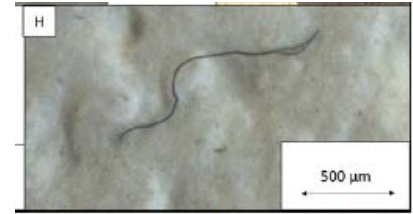
Bar = 200 μm

Human Exposure Estimates (Oral)

Consumable	Size range detected	Most abundant shape	Most abundant polymers detected	Microplastics in consumable	Estimated human microplastic consumption per year
Salt , 8 countries world-wide (Karami et al. 2017)	> 150 µm	fragments fibers	polypropylene polyethylene	1 – 10 particles/kg salt	< 40
Salt , Spain (Iniguez et al. 2017)	30 – 3500 µm	only fibers measured	polyethylene terephthalate	50 – 280 particles/kg salt	< 510
Blue mussels and oysters , Northern Atlantic (Van Cauwenberghe and Janssen, 2014)	5 – >25 µm	Not specified	Not determined	0.42 particles/g tissue	1800 – 11,000
Tap water , 14 countries world-wide (Kosuth et al. 2018)	100 – 5000 µm	fibers >> fragments > films	Not determined	0 – 61 particles/L	5800

- *Are microplastics getting into the human body?*
- Fibers are prevalent

Airborne Microplastics

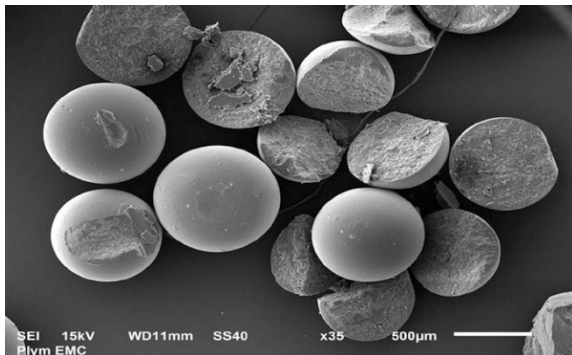


Gasperi et al. 2015

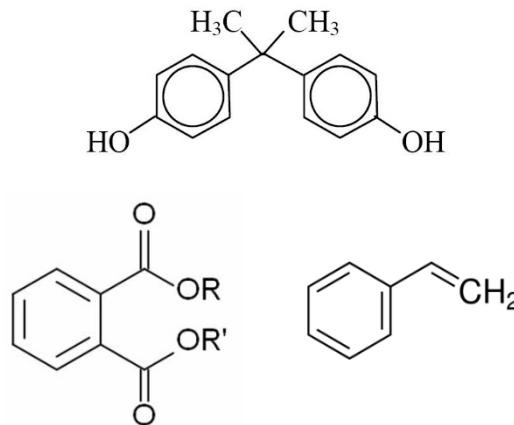
- Atmospheric fallout study (Dris et al. 2015. 12:592)
 - Parisian roof top collection over a 3-month period
 - 118 microplastics $\text{m}^{-2} \text{d}^{-1}$ (range: 29 – 280 microplastics $\text{m}^{-2} \text{d}^{-1}$)
 - 90% of microplastics were fibers
 - 50% between 100 – 1000 μm ; 50% between 1000 – 5000 μm
- ~30% of indoor dust is **plastic microfibers** (Dris et al. 2017. 221:453)
- Sources of airborne microplastics
 - Synthetic textiles (clothing, household items)
 - Land-based application of biosolids (plastics retained in sewage sludge)
- Estimated human exposure from indoor atmospheric fallout
 - **~68,000 microplastic fibers per year** (Catarino et al. 2018. 237:675)

Toxicological Considerations

- Chemical and physical properties, either alone or in combination, make micro/nanoplastics potentially toxic
 - 1) Size
 - 2) Chemical composition
 - 3) Serve as a vector (chemical, biological)

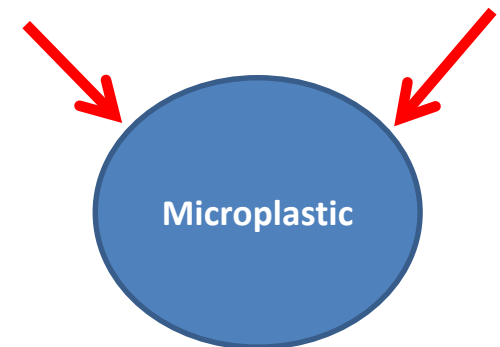


Thompson (2015), In *Marine Anthropogenic Litter*.



POPs
Metals

Bacteria



Size

Size	Description
10 mm	Diameter of large blood vessel (aorta)
5 mm	<u>Upper size limit of microplastics</u>
2.5 mm	Size of a flea
500 μm	Terminal bronchioles
330 μm	Lower size limit of neuston nets
200 μm	Microplastic fragments in a facial scrub
100 μm	Thickness of a sheet of paper
10 μm	Diameter of a capillary (blood, lymphatic)
7 μm	Diameter of red blood cells
5 μm	Microplastic particles in toothpaste
1 μm	Width of anthrax bacterium
100 nm	<u>Upper size limit of nanoplastics</u>
20 nm	Diameter of small viruses
2 nm	Diameter of DNA
1 nm	Diameter of carbon nanotube (single-walled)



Chemical Composition - Monomers

- Plastics are made of **monomers** linked together to form macromolecular chains
- Unreacted **monomers** may leach from polymer

Polymer	Monomer(s)	Health hazard
Polyurethane	Propylene oxide	Mutagenic, possibly carcinogenic to humans
	Ethylene oxide	Mutagenic, carcinogenic to humans
	Toluene-diisocyanate	Irritant
Polycarbonate	Bisphenol A	Endocrine disruption Reproductive and developmental effects
Polystyrene	Styrene	Genotoxic, probably carcinogenic to humans
Polyvinylchloride	Vinyl chloride	Carcinogenic to humans

Chemical Composition - Additives

- **Additives** alter the nature of plastics to increase functionality
- Not bound to the polymer and could leach out of plastic

Additive	Function	Health Hazard
Phthalates	Plasticizers	Endocrine disruption
Triclosan	Antimicrobial	Endocrine disruption
Polybrominated diphenyl ethers	Flame retardants	Endocrine disruption
Alkylphenols	Antioxidant	Endocrine disruption

Vector - Environmental Pollutants

- Microplastics have a high surface area to volume ratio and hydrophobicity
- Adsorb, concentrate, and release **environmental pollutants**

Adsorbed pollutant	Health Hazard
Polychlorinated biphenyls	Carcinogenic to humans
Polycyclic aromatic hydrocarbons	Some are carcinogenic to humans Developmental effects
Organochlorine pesticides	Some are carcinogenic to humans Neurotoxicity Endocrine disruption Reproductive/developmental effects
Cadmium	Carcinogenic to humans Renal toxicity
Chromium	Carcinogenic to humans
Lead	Neurotoxicity

Toxicokinetics

What is the body (potentially) doing to microplastics?

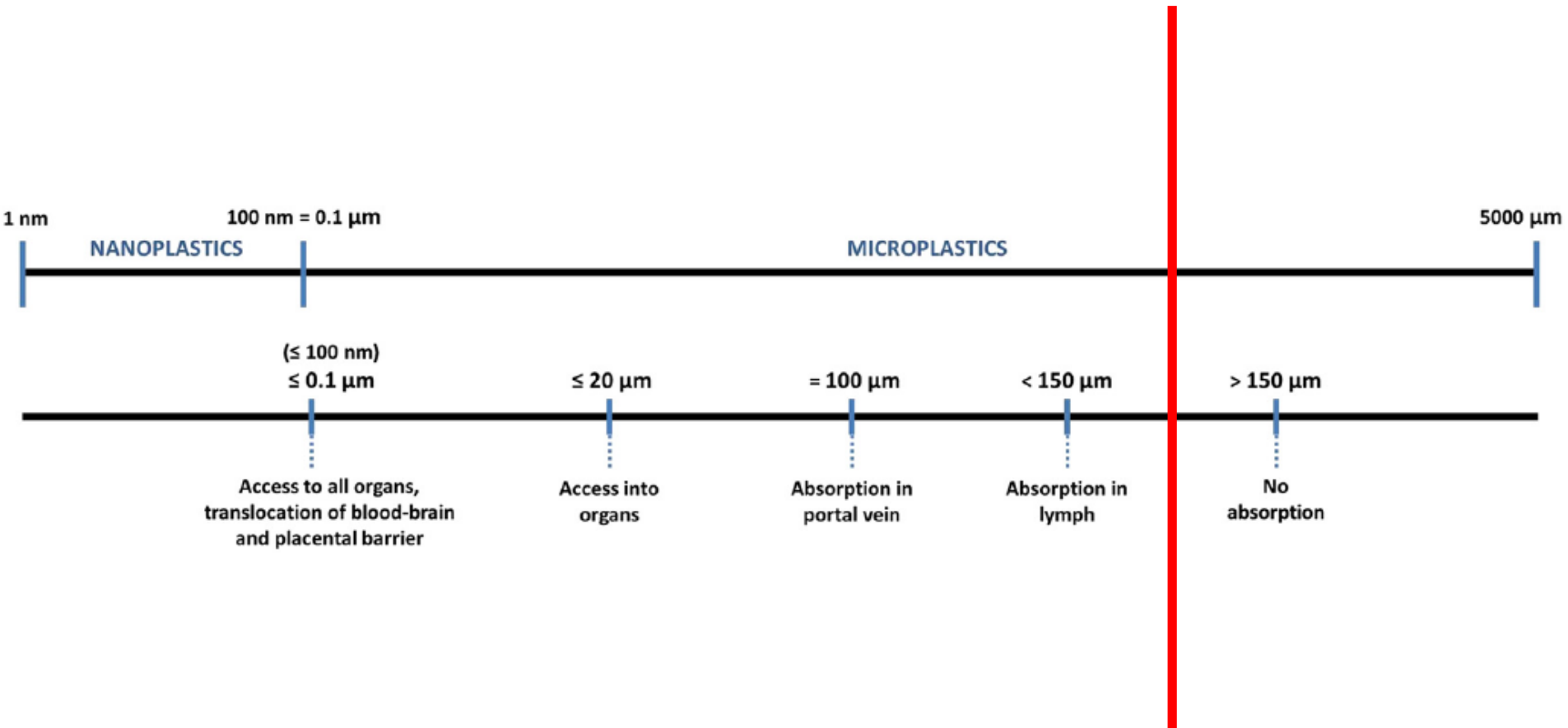
- Absorption (GIT)
- Distribution
- Metabolism
- Excretion

Currently available information

- Limited human data
- Non-human models
- Surrogate materials (e.g., microparticles)
- Not definitive but a good starting point

Toxicokinetics – Size

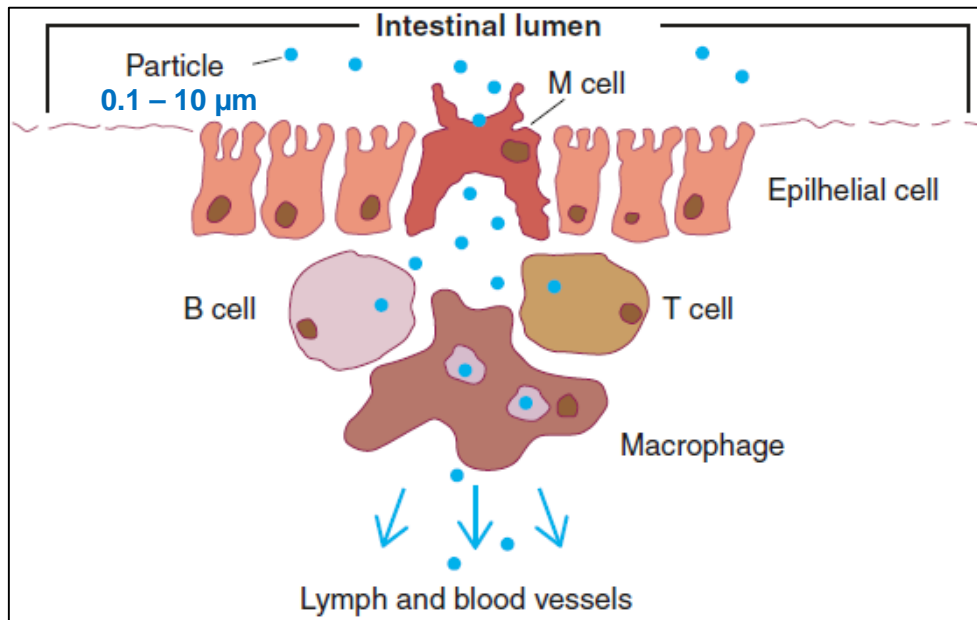
- Predicted sizes for **absorption** and **distribution**



Toxicokinetics - Absorption

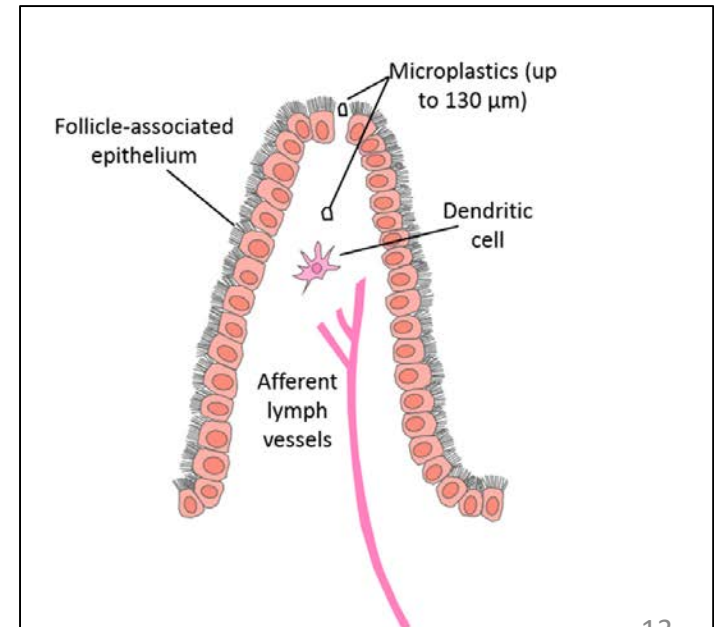
- Many factors likely affect the absorption of microplastics (size, shape, polymer, charge, hydrophilicity, physiological factors, presence of food)
- Predicted to be low: <1% (reviewed in Lusher et al. 2017)
- Major mechanisms: endocytosis and persorption

Endocytosis (Peyer's Patches)



From Galloway 2015. *Marine Anthropogenic Litter*. Chp 13.

Persorption (mechanical kneading)



From Wright and Kelly 2017. 51:6634

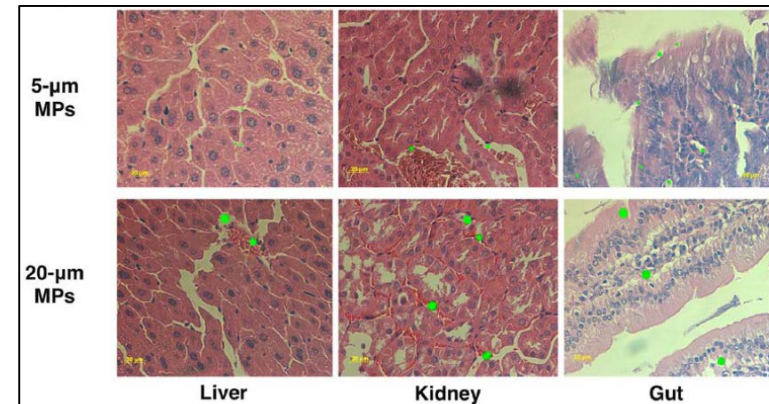
Toxicokinetics - Distribution

Assuming microplastics ingested by humans can cross the GIT, can they reach secondary organs (e.g., liver, muscle, brain)?

- Many factors likely affect the distribution of microplastics (size, shape, polymer, charge, hydrophilicity)

Mouse data (Deng et al. 2017. 7:46687)

- Fluorescently labeled PS (5 or 20 μm)
- Oral gavage for 4 weeks + 1-week recovery



Human arthroplasty data (Urban et al. 2000. 82:457)

- Autopsy samples from individuals with knee or hip replacement
- PE wear particles (1 – 30 μm) found in lymph nodes, liver, and spleen
 - Granular, needle-like, fibers

Toxicokinetics - Metabolism

- Plastic is inert
- Not likely that humans are breaking down plastics
- Some **monomers**, **additives**, and **adsorbed environmental contaminants** require metabolism to form toxic, reactive metabolites
 - Vinyl chloride
 - Styrene
 - Polycyclic aromatic hydrocarbons

Toxicokinetics - Excretion

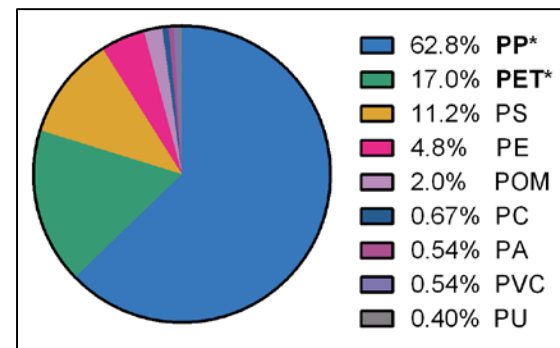
- Microplastics have been found in human stool

Methods

- Population
 - 8 participants from around the world (3 males, 5 females)
 - Age 33–65 yrs old
 - Austria, Finland, United Kingdom, Italy, Japan, Netherlands, Poland, Russia
 - Exclusions: GI disease, recent dental treatment, alcohol abuse, drugs affecting stool
- Exposure assessment
 - Food log 6–7 days prior to stool sample
 - Questionnaires: plastic exposure, alcohol, gum chewing, cosmetics, PET bottle usage
 - ~ 50 g of stool
- Detection
 - Hydrogen peroxide digestion (2 weeks) of samples
 - Separation of solids: 0.05–0.5 mm, > 0.5 mm
 - FT-IR spectroscopy for 10 different polymers (PP, PET, PS, PE, POM, PC, PA, PVC, PU, PMMA)

Results

- Participant behaviors
 - No vegetarians
 - 25% chewed gum
 - 75% ate seafood during observation period
 - 100% had contact with plastic-wrapped food
 - 750 ml/day of beverages from PET containers
- Stool detection
 - 100% of stool samples contained microplastics
 - 20 microplastics/10 g stool (median, 0.05–0.5 mm)
 - ≤ 7 types of plastic found per sample
 - No lab contamination detected
- Polymer frequency



* = detected in 100% of samples

Toxicodynamics

What are microplastics (potentially) doing to the body?

- **No peer-review research has been identified that directly assessed human health effects of environmental microplastics**
- Research areas that may inform human health effects
 - Occupational studies
 - Medical device
 - Animal studies

Toxicodynamics

Occupational studies (inhalation route)

- Presence of respirable synthetic fiber dust (microfibers)
- Industries
 - Synthetic textile (nylon, polyester)
 - Flock (deposition of fiber dust onto substrate)
 - Vinyl chloride/polyvinylchloride
- High concentration exposures but may provide an indication of potential human health effects from other sources (environment, household)
- Reported observations:
 - Decreased lung function
 - Inflammatory responses
 - Flock worker's lung
 - Nasal cancer
 - Lung cancer
 - Cancer at distal sites (GIT)

Toxicodynamics

Medical device (joint replacements)

- Goal: to understand the role of micro-sized plastic particles in joint replacement failure
- Models: whole mouse, mouse cells, human cells

Level of biological organization	Particle type and size	Effect	Reference
Macromolecules	PE 100 nm–30 µm PS 50 nm–4.7 µm PMMA 1 µm–2 µm PC 1 µm–55 µm	DNA damage, changes in gene and protein expression	Gelb <i>et al.</i> , 1994; Brown <i>et al.</i> , 2001; DeHeer <i>et al.</i> , 2001; Gretzer <i>et al.</i> , 2002; Petit <i>et al.</i> , 2002; Ingram <i>et al.</i> , 2004; Clohisy <i>et al.</i> , 2006; Kaufman <i>et al.</i> , 2008; Markel <i>et al.</i> , 2009; Huang <i>et al.</i> , 2010; Hallab <i>et al.</i> , 2012; McGuinness <i>et al.</i> , 2011; Samuelsen <i>et al.</i> , 2009; Smith and Hallab 2010; Pearl <i>et al.</i> , 2011
Organelles*	PMMA 10 µm	more micronuclei	Zhang <i>et al.</i> , 2008
Cells	PS 20 nm–4.7 µm PE 300 nm–10 µm PMMA 2 µm–35 µm PS 20 nm–200 nm PS 60 nm–200 nm	cell clotting, necrosis, apoptosis, proliferation and loss of cell viability Oxidative stress Increased Ca ions	Gelb <i>et al.</i> , 1994; Brown <i>et al.</i> , 2001; Gretzer <i>et al.</i> , 2002; Bernard <i>et al.</i> , 2007; Fröhlich <i>et al.</i> , 2009; Samuelsen <i>et al.</i> , 2009; Hallab <i>et al.</i> , 2012; McGuinness <i>et al.</i> , 2011
Tissues	PE 600 nm–21 µ, PMMA 1 µm–35 µm	inflammation and bone osteolysis	Gelb <i>et al.</i> , 1994; Clohisy <i>et al.</i> , 2006; Markel <i>et al.</i> , 2009; Pearl <i>et al.</i> , 2011
Organs	PMMA 1 µm–10 µm	lesions	Zhang <i>et al.</i> , 2008; Pearl <i>et al.</i> , 2011

Lusher et al. 2017. Table 6.2

PE = polyethylene; PS = polystyrene; PMMA = poly(methyl methacrylate); PC = polycarbonate

Toxicodynamics

Animal studies (Deng et al. 2017. 7:46687)

- Fluorescently labeled PS (5 or 20 μm)
 - Oral gavage for 4 weeks
 - Liver histology: inflammation, lipid droplets
 - Metabolomics: energy metabolism, lipid metabolism, oxidative stress response
-
- Needs replication
 - *What's an appropriate microplastic for exposure?*

NJ Science Advisory Board

Report of the NJDEP-Science Advisory Board

Human Health Impacts of Microplastics and Nanoplastics

Prepared by the Public Health Standing Committee

Approved by the
NJDEP Science Advisory Board

Member of the Public Health Standing Committee include:

Mark Robson, Ph.D., M.P.H., Chairperson

Michael Greenberg, Ph.D.

Gerald Kennedy, M.S.

Howard Kipen, M.D., M.P.H.

Judith Klotz, Dr.P.H.

Mark Maddaloni, Dr.P.H.

Steven Marcus, M.D.

Clifford Weisel, Ph.D.

<http://www.state.nj.us/dep/sab/>

An example of..."state-level environmental protection agencies have begun assessing the public health implications of microplastics and nanoplastics" – Smith et al. (2018. 5:375)

NJ Science Advisory Board

- Charge questions that were addressed
 1. **What are the routes of human exposure?**
 2. **What does the current science indicate in terms of adverse human health effects?**
 3. **Is this issue a concern for New Jersey?**
- Reviewed available peer-review literature, authoritative reports, media reports, and legislation published through September 2015
- Provided responses and recommendations for each charge question

NJ Science Advisory Board

1. What are the routes of human exposure?

- Responses: oral exposure most likely route, potential for inhalation exposure (wave action, atmospheric fallout)
- Recommendations: focus on ecological exposures in NJ (media, aquatic species); monitor on-going research efforts

2. What does the current science indicate in terms of adverse human health effects?

- Responses: plausible that exposure to micro/nanoplastics may cause adverse human health effects (based on ecological observations)
- Recommendations: monitor research in nanoparticle toxicology

3. Is this issue a concern for New Jersey?

- Responses: micro/nanoplastics are a putative issue for New Jersey
- Recommendations: put into perspective of other environmental issues; monitor on-going research efforts

USEPA White Paper

Summary of Expert Discussion Forum on Possible Human Health Risks from Microplastics in the Marine Environment

EPA Forum Convened on April 23, 2014



Marine Pollution Control Branch
Office of Wetlands, Oceans and Watersheds
U.S. Environmental Protection Agency
February 6, 2015

- Purpose was “to discuss available data and studies on the issue of possible human health risks from microplastics in the marine environment” and “to identify data gaps and make suggestions for further study”
- Discussion themes
 - Not enough information to assess possible human health risk from microplastics
 - Persistent, bioaccumulative, and toxic (PBT) chemicals: pathway from microplastics to human tissue, relative contribution to human body burden compared to other media
- Suggested future research
 - Focus on geographical areas with high amounts of plastics to determine extent of exposure to aquatic life and humans (subsistence fishing populations)
 - Investigate occurrence and distribution of microplastics < 300 µm in the environment

Potential Future Research

General

- Assess microplastic exposure from domestic sources: clothing, food packaging, building materials
- Prototypical microplastic versus real-world mixture for exposure

Human exposure

- Assess microplastics in commercial and recreational species
- Biomonitoring for physical presence of microplastics (blood, feces)

Human effects

- Focus research on particles $< 150 \mu\text{m}$
- Susceptible populations (lifestages, bowel disease)
- Effects on gut microbiota

Summary/Conclusions

- ***Are microplastics a risk to human health?***
 - Humans are being exposed to microplastics from domestic, medical, and environmental sources
 - Microplastics from *certain sources* can have effects in humans
 - More research is needed to understand human health effects

Further reading

Barboza LGA, Dick Vethaak A, Lavorante BRBO, Lundebye AK, Guilhermino L. 2018. Marine microplastic debris: an emerging issue for food security, food safety and human health. *Mar Pollut Bull.* 133:336-348.

Bouwmeester H, Hollman PC, Peters RJ. 2015. Potential health impact of environmentally released micro- and nanoplastics in the human food production chain: experiences from nanotoxicology. *Environ Sci Technol.* 49:8932-47.

Galloway TS. 2015. Micro- and nano-plastics and human health. In *Marine Anthropogenic Litter*. eds Bergmann M, Gutow L, and Klages M. Springer.

Lusher A, Hollman P, and Mendoza-Hill J. 2017. Risk profiling of microplastics in aquaculture and fishery products. In *Microplastics in Fisheries and Aquaculture: Status of Knowledge on Their Occurrence and Implications for Aquatic Organisms and Food Safety*. Food and Agriculture Organization of the United Nations. Technical paper 615.

Prata JC. 2018. Airborne microplastics: Consequences to human health? *Environ Pollut. Mar*;234:115-126.

Rist S, Carney Almroth B, Hartmann NB, Karlsson TM. 2018. A critical perspective on early communications concerning human health aspects of microplastics. *Sci Total Environ.* 626:720-726.

Wright SL, Kelly FJ. 2017. Plastic and human health: a micro issue? *Environ Sci Technol.* 51:6634-6647.

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