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Identifying Research to Evaluate Exposures to Microplastics

Editor's Note: As part of our continued effort to highlight innovative approaches to improve the health and environment of communities, the *Journal* is pleased to publish regular columns from the Agency for Toxic Substances and Disease Registry (ATSDR) at the Centers for Disease Control and Prevention (CDC). ATSDR serves the public by using the best science, taking responsive public health actions, and providing trusted health information to prevent harmful exposures and diseases related to toxic substances. The purpose of this column is to inform readers of ATSDR's activities and initiatives to better understand the relationship between exposure to hazardous substances in the environment, its impact on human health, and how to protect public health.

The findings and conclusions in this column are those of the authors and do not necessarily represent the official position of CDC, ATSDR, and the National Center for Environmental Health.

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Plastics are a group of useful chemicals that have increased in usage since the 1950s (Miranda et al., 2020). Plastics are stable regarding both temperature resistance and chemical interactivity. Due to of these properties, plastics are utilized in a variety of health products such as toothbrushes, break-resistant beverage containers, and intravenous tubing. Although plastics are extremely useful, they also break down in the environment and present a source of exposure to humans in the form of microplastics. A microplastic is commonly defined as a plastic with any dimension <5 µm (Güven et al., 2017; Stapleton, 2019). Researchers have defined a smaller group of plastics as nanoplastics with a size range from 1 to 1,000 nm (Gigault et al., 2018). Here we will retain the term microplastics to include all plastic particles <5 µm.

To address the emerging public health concerns for exposure to microplastics, an interdisciplinary working group was formed, combining staff from the National Center for Environmental Health (NCEH) and Agency for Toxic Substances and Disease Registry (ATSDR). NCEH has taken the lead on investigating microplastics in drinking water. This work is consistent with its other efforts to provide safe water support to local and state health departments to address risks to human health. ATSDR has evaluated whether exposures to microplastics in the environment are hazardous in alignment with its mandate to evaluate potential health effects of hazardous substances in the environment.

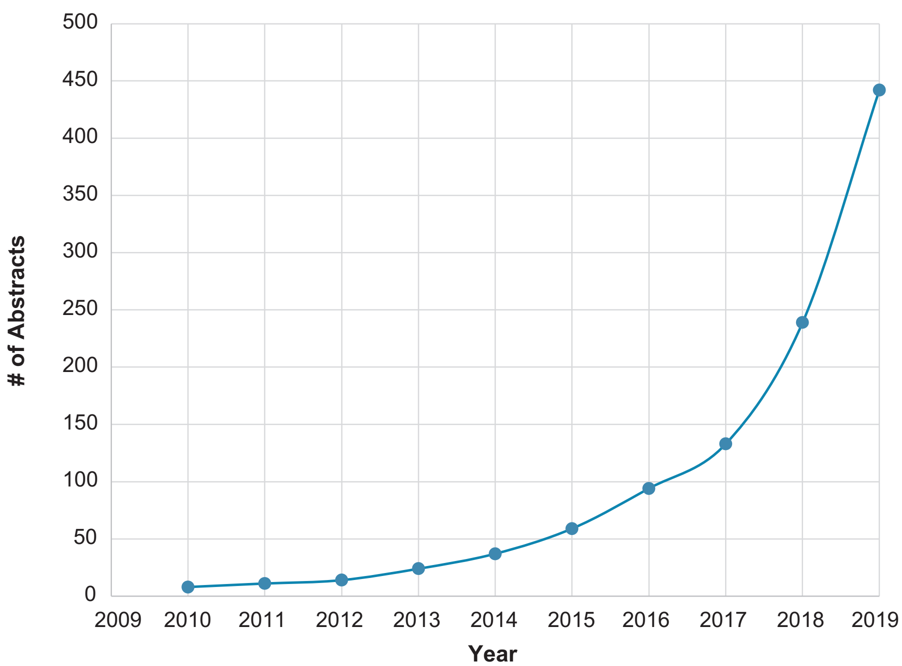
The NCEH/ATSDR microplastics working group has organized the literature on microplastics to understand and characterize human risk and exposure from microplastics. The group has identified major data gaps related to exposure to microplastics in air and water (Zarus, 2020), reviewed efforts to evaluate occupational exposures to microplastics (Zarus, Zarate-Bermudez, et al. 2020), and provided an overview of the transport of microplastics in the environment (Carroll et al., 2020). The group is also developing standardized methods for sample collection and biomonitoring (Muianga et al., 2021; Zarus, Muianga, et al., 2020). The workgroup is currently involved in a series of additional reviews to address various public health issues, three of which are underway. This column is a summary of six of the reviews, grouped according to the following criteria: exposure, effects, and data gaps.

Literature Reviews

The microplastics working group conducted a series of literature searches during 2019–2022 on any topic related to microplastics. Thousands of articles were identified. Figure 1 shows a time series of published literature from 2010–2019. Most published literature occurred after 2015. Team members were assigned a group of documents to review. A scoping review orga-

FIGURE **1**

Time Series of Published Microplastic Articles Identified in Literature Review, 2010–2019



Source: Zarus, Casillas, et al. 2021.

nized the literature into three broad categories: environmental, adsorption and absorption, and human exposure toxicology and health. Much of the published literature was related to the environment. Figure 2 shows the results of one reviewer (Webb et. al., 2021). Publications most frequently addressed questions related to microplastics in water more than any other environmental media, which was consistent with all staff reviews. The higher focus on water is consistent with the early availability of sampling methodologies in water for ecologic purposes (National Oceanic and Atmospheric Administration, 2013). These methods were applied to study ocean plastics and then to study plastics in fish, which left many questions regarding public health implications for fish consumption.

Quantifying Human Exposure

ATSDR (2022) applied its health assessment process to published environmental data to estimate human exposures (Zarus, Muianga, et al., 2021). This assessment included human exposure via three main routes: ingestion, inhalation, and absorption. ATSDR applied relevant human ingestion and inhalation rates to calculate exposure rates. Microplastics in seafoods could amount to thousands of microplastic particles ingested per day. Although exposures to the microplastics measured in water, air, and food additives appeared to be much less than in seafood, the sampling methods limited the size of microplastics able to be detected in those media. Packaging, as with plastic tea bags, appeared to increase microplastic exposure, but packaging studies used different analytical methods than those used for most foods. Table 1 summarizes the published environmental microplastic data to assess human exposures. The data gaps identified in the exposure media were used to inform a workshop and follow-up work involving international scientists (Zarus, Casillas, et al., 2021).

Assessing Effects of Human Exposure

Reviews showed target organs and systems that microplastics can affect, including the immune system, respiratory system, hepatic system, and gastrointestinal (GI) tract (Zarus, Muianga, et al., 2021; Zarus, Zarate-Bermudez, et al., 2020). Importantly, ATSDR found that documented clinical effects were not associated with the term "microplastics" but rather exposure to specific synthetic substances.

Direct exposure to microplastics resulted in lung effects in animals and, because of occupational exposures, in humans. Immune system effects included polyethylene translocating in the lymph system from implants and a foreign body response. Neurologic system effects included polystyrene affecting neurologic mouse cells and polyethylene associated with human dopamine levels. Microplastics were detected in the GI tracts and feces of environmentally exposed individuals and worker studies identified GI health effects. Studies of the hepatic system included an associated health effect in workers. Table 2 summarizes data and data gaps germane to human exposures to microplastics and associated effects. While exposures to many populations are demonstrated, clear clinical effects were only observed in workers or patients with plastic implants. Many data gaps exist relating animal studies to human exposures.

Identifying Critical Data Gaps

Although microplastic literature heavily favored an environmental focus, data gaps remain within that arena. Very few studies examine the most bioavailable plastics—those plastics smaller than 10 µm (Table 1). Methods in the marine environment, while more standardized than other media, lack inclusion of the smaller particles that can move within cells. Other environmental media lack method standardization. Additionally, few studies define how microplastics behave in the atmosphere and in the sediment. ATSDR identified several pressing data gaps related to identifying microplastics exposure and toxicity to humans. A general list of the data gaps that need to be addressed to form a more complete picture of microplastics toxicity and exposure to humans is available in Table 2.

In December 2021, ATSDR led a session to address some of the health-related data gaps within the Asian-Pacific Economic Cooperation Workshop on Nanoplastics in Marine Debris (Zarus, Casillas, et al., 2021). During this session, presenters provided new data identifying unique effects of polystyrene, polyvinyl chloride, and acrylic on lung cells, and a means to assess the effects of microplastic exposures (Goodman et al., 2021; Mahadevan & Valiyaveettil, 2021; Mumtaz & Gehle, 2021). The direct cell dosing studies cannot be used to assess human health implications because they incompletely characterize human exposures. They do suggest, however, a need for follow-up studies. A current review at ATSDR is providing a statistical analysis of the data in Table 2 to assist in prioritizing the data needs.

Conclusion

The study of microplastics is relatively new, with researchers quickly responding to the published data gaps. ATSDR and NCEH are conducting scoping reviews on thousands of published research studies on microplastics. The lack of microplastic-specific information before 2015 does not exclude the important work that had been conducted prior to 2015, as prior to that date much work was conducted on specific plastic substances such as nylon, polyethylene, polyvinyl chloride, etc.

General conclusions that can be made now include the following:

- Most microplastics research has been focused on the environment, specifically that of oceans, lakes, and rivers.
- Most people are exposed to microplastics in air, water, and foods.
- Some microplastics translocate within our bodies.
- Some microplastics carry other pollutants.
- Clear clinical effects have only been demonstrated in occupational settings.
- Cell studies that find unique effects currently cannot be applied to understand environmental exposures.

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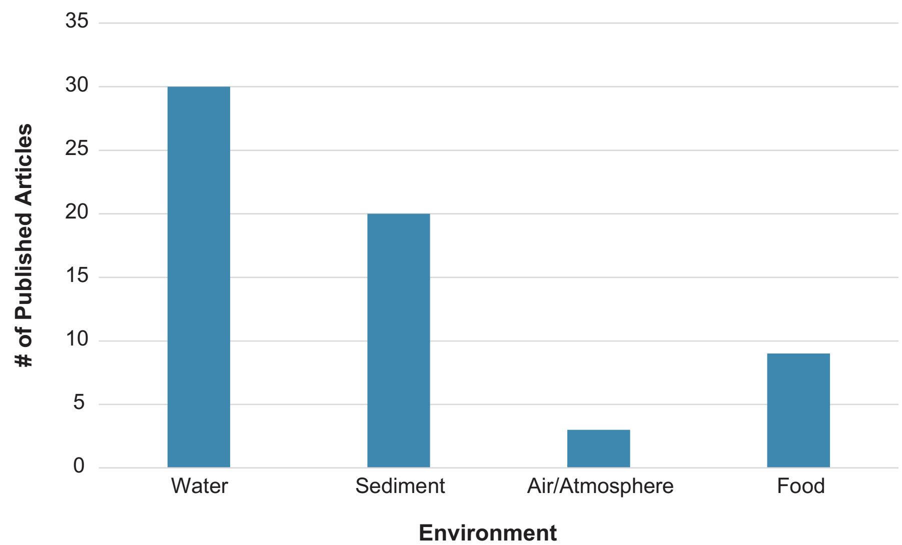
FIGURE **2**

Published Articles on Microplastics in the Environment From One Reviewer



Source: Webb et al., 2021.

TABLE **1**

Published Environmental Microplastic Data to Assess Human Exposures

Exposure Element	Evidence	Microplastic Data	Critical Data Needs
Air	Measured directly	>10 µm particles characterized for indoor and outdoor air	Fine particles (<10 µm) need characterization
Seafood	Measured in gastro-intestinal systems of fish, crabs, and bivalves	>10 µm particles characterized in gastro-intestinal systems mostly	Fine particles (<10 µm) need characterization
Drinking water and beverages	Measured directly	>10 µm particles characterized in many cities	Fine particles (<10 µm) need characterization
Seasonings	Salt, sugar, honey	>10 µm particles characterized	Fine particles (<10 µm) need characterization
Vegetables not characterized	In soils and plankton	None	Full characterization is needed
Meats not characterized	In soils and seafood scraps, phthalates in mammals	None	Full characterization is needed

Note. The table is shaded to assist in identifying the largest data gaps for assessing microplastic exposure and effect. Orange identifies the largest data needs, yellow identifies a need for further characterization, and green identifies there is sufficient characterization to demonstrate exposure from an element. Proof of exposure does not connote evidence is sufficient to characterize exposures. Table modified from Zarus, Muianga, et al., 2021.

TABLE **2**

Evidence of Data and Data Gaps Relevant to Human Exposures and Effects

Uptake and Absorption	Evidence	Microplastics Data	Critical Data Needs
Lungs	Measured directly in workers, along with health effects, and in animals	Measured in workers and in air	Not studied in nonworkers
Immune system	Polyethylene was found to translocate lymphatics in implant patients and related to immune response	Measured translocation in implant patients; found in lymph nodes of workers	Not measured in the general population
Neurologic system	Polystyrene alters neurologic mouse cells only; polyethylene association with dopamine in humans	Measured in biota, but effects might be associated with nano size	Not measured in the general population; full pathways of uptake not demonstrated
Gastrointestinal (GI) system	Measured in feces of general population; implied by association with health effects in workers; GI cancers	Measured translocation in animals after insertion; cancers associated with the work environment	Human data on GI absorption not known but associated with effects; feces microplastics and urine phthalates are nonspecific indicators
Liver	Implied by association with health effects in workers only	Injected microparticles circulated to liver; also measured in liver and spleen of implant patients	Not measured in workers, animals, or the general population but found in implant patients
Biomagnification of other toxicants	Measured directly as a factor >1x in marine animals, but no support for great magnification is demonstrated	Measurements in marine environment and in fish GI tracts indicate a decrease in the trophic levels, not an increase; therefore, the increase to humans is expected to be slight	Data in human food supply are needed; however, total exposure to many persistent pollutants occurs routinely

Note. The table is shaded to assist in identifying the largest data gaps for assessing microplastic exposure and effect. Yellow identifies a need for further characterization and green identifies there is sufficient characterization to demonstrate uptake and absorption is occurring. While evidence of uptake and absorption has been demonstrated, it is insufficient to fully link associated effects with exposure dose. Table modified from Zarus, Muianga, et al., 2021.

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