Humans are exposed to different types of fibers and particles, including microplastics; the potential health effects of microplastics are largely unknown.



TOXICOLOGY

# Microplastics and human health

## Knowledge gaps should be addressed to ascertain the health risks of microplastics

By **A. Dick Vethaak**[1,2] and **Juliette Legler**[3]

The ubiquity of microplastics (plastic particles <5 mm, including nano-sized plastics <1 μm) in the global biosphere raises increasing concerns about their implications for human health (*1*–*3*). Recent evidence indicates that humans constantly inhale and ingest microplastics; however, whether these contaminants pose a substantial risk to human health is far from understood. The lack of crucial data on exposure and hazard represents key knowledge gaps that need to be addressed to move forward.

Microplastics are created by the weathering and breakdown of plastic objects, car tires, clothing, paint coatings, and leakage of preproduction pellets and powders. They may also be intentionally added to daily-life products (e.g., cosmetics and abrasive cleaners) (*1*, *2*). Microplastics represent a highly diverse class of contaminants spanning five orders of magnitude in size, are of various shapes (e.g., spheres, fragments, fibers), and have a complex composition, including polymeric materials and mixtures of chemicals (residual monomers, additives, and hydrophobic environmental contaminants) (*4*–*6*). Furthermore, biofilms growing on microplastics may be a source of harmful microorganisms (*2*, *7*). Their ubiquity in the environment raises serious concerns about their effects on wildlife and ecosystems (*1*), but what are their effects on human health?

Microplastics may enter the human body through both inhalation and ingestion, potentially causing health effects (see the figure). A parallel can be drawn with particulate air pollution: Small particles (<2.5 μm), such as those from diesel exhaust, are capable of crossing cell membranes and triggering oxidative stress and inflammation, and have been linked with increased risk of death from cardiovascular and respiratory diseases or lung cancer (*3*). This parallel provides ample incentive to gather more information on the potential risk of microplastic particles.

A major issue when determining the risks of microplastics to human health is the lack of information on human exposure. Adequate analytical tools to sample, isolate, detect, quantify, and characterize small microplastics (<10 μm), especially nano-sized plastic particles, are urgently needed. External exposure estimates comprise limited and highly variable data of mainly large particles (>10 to 50 μm), with poor standardization and quality control measures, hampering a comprehensive exposure assessment (*1*, *8*). Nevertheless, a growing body of evidence suggests widespread exposure to microplastics from various foods, drinking water, and air (*1*, *9*, *10*).

Reported concentrations of microplastics in tap and bottled water vary between 0 and $10^4$ particles/liter, with generally greater particle counts for small-sized microplastics (*8*). The first atmospheric measurements of larger-sized, predominantly fibrous microplastics indicate that plastic particles are a relevant component of fine dust, with, for example, deposition rates in central London ranging between 575 and 1008 microplastics per square meter per day (*9*). Increased exposure through indoor air, direct swallowing of house dust or dust settling on food (*10*), and direct exposure to particles released from plastic food containers or bottles, such as polypropylene infant feeding bottles (*11*), are of special concern. Larger microplastics are likely excreted through feces, or after deposition in the respiratory tract or lungs through mucociliary clearance into the gut (*1*, *2*). Given the methodological limitations and measurement bias toward larger particles, existing analyses probably underestimate human external exposure and generally do not include the fraction of smaller-sized particles <10 μm, which are likely more relevant to toxicity (*1*, *12*). Notably, internal exposure measurements of plastic particles in human body fluids and tissues are still in their infancy.

A better understanding of the ability of microplastics to cross the epithelial barriers of the airway, gastrointestinal tract, and skin is needed to reduce the current uncertainty in the human risk assessment of microplastics. Limited in vitro and in vivo data suggest that only small fractions of administered microplastics are capable of crossing epithelial barriers of lungs and intestines, with specific uptake profiles and generally increasing uptake efficiency with decreasing particle size (*2*). This low proportion of particle uptake is not necessarily unimportant when considering life-long exposure and because of possible accumulation in tissues and organs. Studies with human cells in culture, and in rodents and aquatic species indicate translocation of microplastics <10 μm from

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Corrected 19 February 2021. See full text.

the gut cavity to the lymph and circulatory systems, causing systemic exposure and accumulation in tissues including liver, kidney, and brain (*12*). Although the smallest particles (<0.1 μm) may be capable of accessing all organs, crossing cell membranes (*12*), the placenta (*13*), and also the brain (*14*), major knowledge gaps regarding absorption, distribution, metabolism, and excretion (ADME) still exist. Whether there are dose-dependent effects of microplastics in humans also remains unknown.

Once in contact with epithelial linings in the lung or intestine, or after being internalized, microplastics may cause physical, chemical, and microbiological toxicity, which could also act cumulatively. Several in vitro (i.e., human cell culture) and in vivo rodent studies indicate the potential of inhaled or ingested microplastics to cause a variety of biological effects, including physical (particle) toxicity, leading to oxidative stress, secretion of cytokines, cellular damage, inflammatory and immune reactions, and DNA damage, as well as neurotoxic and metabolic effects (*12*). The observed effects are usually triggered at high exposure concentrations of microplastics, and these experiments use a limited number of pristine, commercially available particle types, which are inconsistent with those encountered in the environment. Furthermore, chemical contamination of these test particles cannot always be excluded. Similar to the effects observed in ambient particle exposure studies, epidemiological studies have reported lung injuries, including inflammation, fibrosis, and allergy, among workers in the plastic and textile industry who are exposed to high amounts of plastic fibrous dust (*2*).

Chemical toxicity may be caused by microplastics acting as vectors to transfer exogenous hazardous chemicals, proteins, and toxins present in or on the particles into the body (*1*, *5*, *6*). However, this "Trojan horse" effect is understudied with little knowledge of the role of nanosized microplastics, which are more effective at crossing biological membranes and have increased surface area for chemical reactivity than larger-sized microplastics. Some studies suggest that aquatic microplastics may act as vectors of microbiological toxicity, carrying biofilm-associated opportunistic bacterial pathogens and antibiotic resistance genes that may interact with gut microbiota (*15*). In-depth research on the stability of microbial contaminants within the human body is required to further clarify this. The possibility that microplastics act as carriers of other potential pathogens, such as fungi and viruses, also deserves attention. More research is urgently needed to fully understand the potential toxicity, underlying mechanisms, and long-term effects of microplastics under real life conditions.

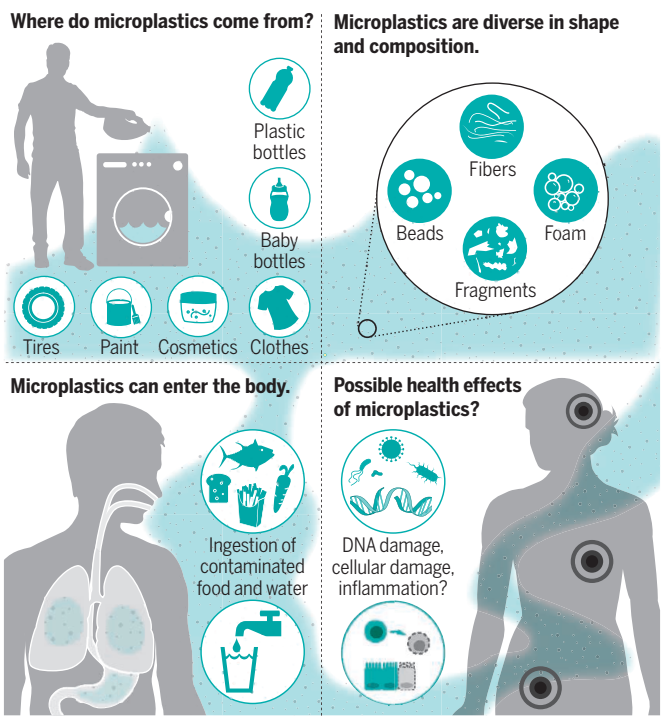
An additional intriguing, yet understudied, but potentially hazardous property of microplastics is the presence of an eco- or biocorona, i.e., biomolecules and other substances on the surface of the plastic particle, which may influence particle uptake, fate, and effects (*6*, *13*). The heterogeneous composition of the eco- or biocorona is determined by the physicochemical properties of the microplastic and complex particle interactions with both the environment (comprising natural matter, biomolecules, chemical contaminants, and microorganisms) and the human body (adsorbed lipid and proteins) (*6*, *7*, *13*). Before crossing the epithelial barriers in the lung and intestine, microplastics are trapped in the mucus layer covering the cells, whereas ingested particles have to pass through acidic conditions in the stomach and intestinal lumen. The role of the changing composition of the eco- or biocorona acquired by microparticles, from the outside to the inside of the body, across tissue barriers, and the underlying mechanisms in mediating uptake and toxicity are poorly understood and deserve more study.

The major knowledge gaps outlined above prevent a thorough assessment of the health risks of microplastic exposure for humans. However, ongoing research can help progress our understanding. Technological advancements for particle analysis of microplastics, especially nano-sized microplastics, in relevant human body fluids and tissues are anticipated within the next few years. In general, microplastics are thought to affect human health as a function of their properties, such as chemical composition, size, shape, and surface charge (*1*, *2*, *6*). Improved characterization of test particles and research that reflects real environments are needed, for example, by examining environmentally weathered flakes and fibers in addition to the pristine polystyrene spheres often used now.

Additionally, given their physicochemical similarities (e.g., poor solubility, high persistence, wide size range, and complex nature), there are important parallels between microplastics and much-studied nanomaterials and particulate air pollution. Therefore, research on plastic particles may build on existing knowledge and lessons learned from research on nanomaterials; and predictions from kinetics, toxicological, and epidemiological data associated with particulate air pollution, notably the effects of exposure to mineral dust particles and soot particles from combustion sources. To assess the extent to which any effects found are specific to microplastics, it would be useful to compare the effects of different standard polymer reference materials with well-studied positive controls, such as soot particles, engineered nonplastic nanomaterials, silica particles, and natural polymers. Furthermore, important knowledge on environmental microplastics can be mined from the use of polymeric particles in drug delivery systems and particles abraded from plastic prosthetic implants (*2*).

## What are the effects of microplastics in humans?

Microplastics (plastic particles <5 mm) can come from the breakdown of plastic objects, car tires, and clothing, but also from their use in cosmetics and other applications. They have diverse shapes and encompass a suite of chemical and biological constituents. Microplastics can enter the human body through ingestion and inhalation where they may be taken up in various organs and might affect health, for example, by damaging cells or inducing inflammatory and immune reactions.

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Every day, humans are exposed to a wide range of natural and manufactured particles, with particulate air pollution recognized as one of the world's leading environmental risk factors for disease. It is crucial to understand the role of microplastics and their contribution to total ambient particle exposure to evaluate their potential contribution to global disease burdens. Owing to their persistence, wide size range, and complex nature, microplastics may exhibit distinct particle properties with a different and broader toxicity profile compared to those of other ambient particles. To date, pressing microplastic-related health issues such as internal exposure; ADME processes, including the effect of the eco- or biocorona; interaction with the immune system; whether nanosized plastics can affect the placenta, fetus, and brain; and how environmental microplastics differ from other ambient natural and engineered nanoparticles are largely unexplored. Pioneering interdisciplinary research programs (such as Microplastics & Health in the Netherlands and the European Union Horizon 2020 research program) are beginning to resolve some of these issues, which are fundamental to innovation, evidence-based policy-making, and strategies to improve risk management. Multidisciplinary research efforts, involving scientists from environmental and medical sectors as well as polymer scientists, are needed to tackle this potential health hazard. Comprehensive risk assessment is still far away, but the major research gaps should be addressed now to support timely decision-making on health policies and mitigation strategies. ■


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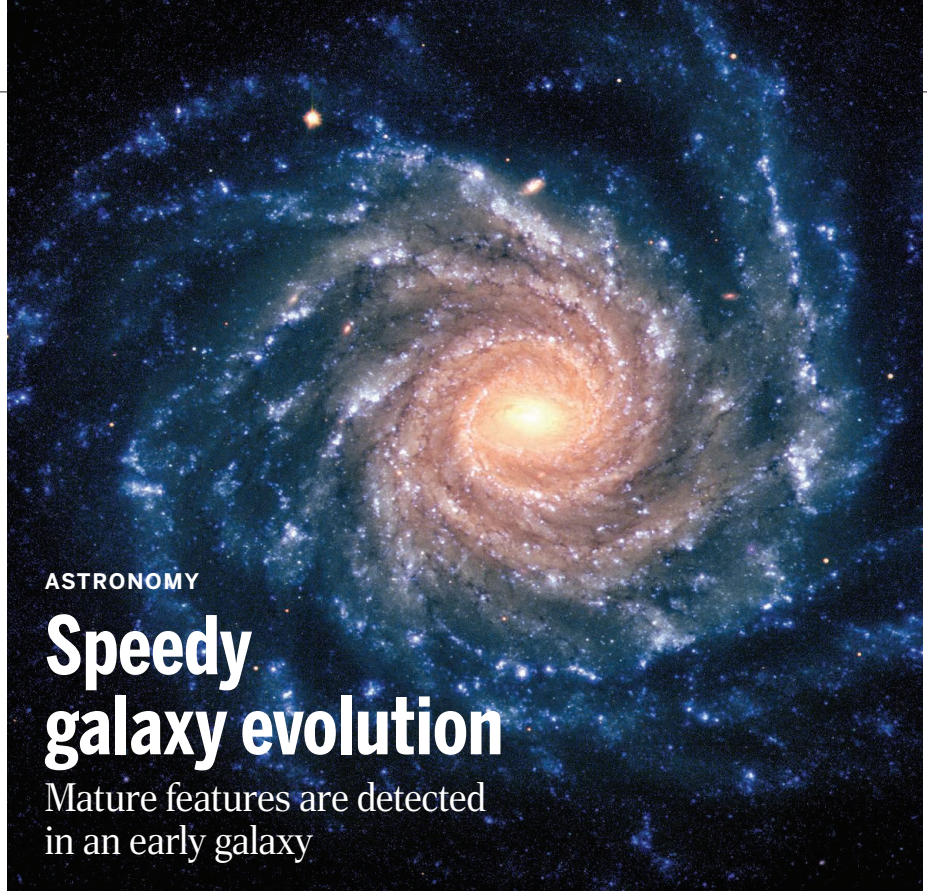
### ACKNOWLEDGMENTS

The authors receive financial support from The Netherlands Organisation for Health Research and Development (ZonMw). We thank F. Pierik, program leader ZonMw Microplastics & Health program, and all collaborators in this program for helpful discussions.

10.1126/science.abe5041

ASTRONOMY

# Speedy galaxy evolution

## Mature features are detected in an early galaxy

An image of galaxy NGC 1232 (September 1998) shows spiral arms and central red bulge, the hallmarks of maturity.

*By* **Julie Wardlow**

The processes that transformed small, turbulent, relatively unstructured protogalaxies into rotating spiral or giant elliptical galaxies are not well understood. Most galaxies are expected to go through a spiral-like phase, maturing into an elliptical structure. Many local spiral galaxies have a classic rotating disk of young stars as well as a "bulge" of older red stars at their centers; these two features are considered to be signatures of galaxies that have evolved from their original primordial forms. Unfortunately, these features are challenging to directly detect, particularly in the very distant (i.e., early) Universe. On page 713 of this issue, Lelli *et al.* (*1*) report a galaxy that had evolved features (both a disk and a bulge) when only 1.2 billion years had elapsed since the Big Bang (~12.5 billion years ago) (see the figure). This finding suggests that the processes that generate the key features of a mature galaxy arose more rapidly than has been thought.

Theoretical simulations suggest that primordial galaxies started to form shortly after the Big Bang and are expected to merge together through gravity. They form increasingly large but somewhat chaotic structures (*2*) that may have some rotation but must also eventually form bulges of old stars. The mechanism of bulge formation requires additional observations to constrain the model.

There are two main theories for forming a concentrated population of old stars: galaxy mergers and internal instabilities. Mergers cause huge gravitational disturbances that can compress cold gas (the fuel for new stars), triggering huge but short-lived bursts of star formation. Similarly, the distant Universe was a chaotic place, and it is thought that early galaxies were often gravitationally unstable such that internal stochasticity could have triggered similar dynamical disturbances and compressions of gas leading to an intense starburst. In both scenarios, after the gravitational disturbance, the cold gas fuel for star formation is rapidly exhausted, leading to an aging of the central stellar population along with a relaxation of the dynamics. Because both scenarios lead to similar theoretical outcomes, the question of whether galaxy bulges form from stochastic internal processes or as the result of galaxy mergers requires observations to answer the question of how bulges emerge.

Although it is clear that distant galaxies tend to have more irregular and "clumpy" morphologies than local galaxies, these clumps can be interpreted as evidence for both massive star-forming regions (i.e., sec-

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Corrected 19 February 2021. See full text.

Published by AAAS

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*Science*, **371** (6530), .
DOI: 10.1126/science.abe5041