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Posted Date: 8 December 2023

doi: 10.20944/preprints202312.0565.v1

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What Health Concerns Could Micro and Nanoplastics Pose for Infants? A Review

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Abstract: Microplastics and nanoplastics (MP/NPs) have been found everywhere they have been searched. On the top of Everest, in the Mariana Trench, on the clouds e recently, microplastics have been discovered in the human placenta, meconium and babies' feces. In this review we explain what the consequences of the presence of these pollutants in fetuses and newborns are, with particular attention to human breastfeeding. Finally, we outline the possible political and social solutions to the problem of plastic overproduction that characterizes the modern world.

Keywords: plastic; microplastics; nanoplastics; newborns; breastfeeding; plastic products manufacturers; human behaviors

The problem

MP/NPs can be measured in human blood using various methods, gas chromatography/mass spectrometry for example (1) or other types of microscopic analysis, such as Raman microscopy. Flow cytometry it is probably the best method to detect micro and nanoplastics in the blood. Probably 0.1-0.3% of plastics in the blood are MPs, while the vast majority are NPs (2).

However, as far as we am aware there are still no commercial kits available to the end user at a reasonable cost and outside of scientific studies. Moreover, the paucity of studies on the subject does not allow to draw levels of "normality" of the quantity and quality of MPs and NPs present (probably in all of us there are MP/NPs. Only that the amount varies according to the level of exposure). However, population studies of this kind are necessary. This will make it possible to have commercial kits available that can be used after understanding the statistical distribution of the quantity and quality of MPs and NPs present in human blood.

Science needs time to prove observations with evidence and this could take a long time. In humans we do not yet have definitive evidence of toxic effects of microplastics. However, there is very clear evidence in experimental animals that microplastics and nanoplastics that enter the body through respiration, skin and gastrointestinal tract, reach all the main tissues, organs and systems, where they can determine toxic and harmful effects.

In an interesting study, Deng *et al*. (3) used fluorescent and pristine polystyrene microplastic particles with two diameters (5 μm and 20 μm) to investigate the tissue distribution, accumulation, and tissue-specific health risk of MPs in mice. MPs accumulated in the liver, kidney, and gut, with a tissue-accumulation kinetics and distribution pattern that was strongly dependent on the MPs particle size. Analyses of multiple biochemical biomarkers and metabolomic profiles suggested that MPs exposure induced disturbance of energy and lipid metabolism as well as oxidative stress.

Jeong B et al (4) in another intersting study showed that maternal administration of polystyrene nanoplastic in mice during gestation and lactating periods altered the functioning of neural cell compositions and brain histology in progeny. Furthermore, polystyrene nanoplastic induced molecular and functional defects also in cultured neural cells *in vitro*. The abnormal brain

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development caused by exposure to high concentrations of polystyrene nanoplastic results in neurophysiological and cognitive deficits in a gender-specific manner.

The effects of plastic are very important, especially on the central nervous system. Adult offspring of female mice (L-DE-71 F1) exhibit short- and long-term deficient social recognition, reduced sociability, and increased repetitive behavior when they were exposed to the Polybrominated diphenyl ethers (5) these effects are very similar to those found in autistic humans. Ultimately, exposure to Polybrominated diphenyl ethers, during intrauterine development produces neurochemical, olfactory, and behavioral processes that are relevant and very similar to those of autism spectrum disorders (ASD) in humans. These effects can reprogram early neurological development within central memory and social networks. Importantly, autism spectrum disorders prevalence in humans has dramatically increased in recent years.

Oral administration of monodispersed polystyrene causes damage to the visceral organs in mice. The main toxicities are the damage to the liver function and the lipid metabolism abnormality. Chronic exposure to monodispersed polystyrene significantly increases plasma glucose levels and ROS levels but does not influence plasma insulin secretion. Ultimately oral administration of monodispersed polystyrene increases ROS, liver triglycerides and determines the accumulation of cholesterol in mice (6).

In summary, also in humans the presence of MP/NPs in term placenta samples, could contribute to the activation of pathological traits, such as oxidative stress, apoptosis, and inflammation, characteristic of metabolic disorders, which underlie future diseases, such as obesity, diabetes, metabolic syndrome, and many other pathologies, which have their roots in oxidative stress damage and organelle dysfunction, But while this is a certainty in laboratory animals, in humans this evidence is not yet there. This fact explains well the previous evaluations of the European Food Safety Authority (7).

Microplastics have been discovered in the human placenta, meconium and babies feces (8-9-10-11).

Yet, the impacts of exposure to plastic particles during early windows of vulnerability are almost entirely unknown. Our lack of knowledge of the health impacts of nano- and microplastics and the chemicals they contain, prevents evidence-based assessment and effective management of potential health risks from exposure to plastics. The fundamental questions remain open: to what extent are humans exposed to nano and micro plastics, especially during pregnancy and the first years of life? And what are the long-term effects on human health?

We discovered plastic in human placentas, and we were able to understand which kind of plastic it was, although not in all cases, because plastic as well as microplastics, contain a huge amount of additives, that can make them difficult to identify even whit Raman microscopy. The presence of these additives makes it extremely complex to predict which diseases will arise in the future of children contaminated with plastic, because there is not only the role of plastic that changes the epigenetic expression of many proteins, but also the role of all these additives that are really numerous, so we are trying to enter into an extraordinary complexity.

The issue, however, is not "only" plastic. The chemicals present in plastic products, including for example phthalates and bisphenol A (BPA) and polyvinyl alcohol act, in fact, as endocrine disruptors. Endocrine disruptors are similar in structure to natural sex hormones and interfere with their normal functioning. In children, who are still growing and developing, this is a big problem.

After the first study the further curiosity that came to us was where plastic could be located. Inside the cellular compartment? Or nearby? In which cells? How could plastic possibly morphologically alter cellular compartment components?

Our team succeeded in locating compatible particles like microplastics in all the compartments of placental villi. And we note a correlation between the presence of these particles and an alteration in placental cells (endoplasmic reticulum and mitochondria).

We demonstrated morphological alterations with a dose-response effect in endocellular components such as endoplasmic reticulum and mitochondria, where microplastic particles were present. These morphological alterations are probably the cause of the epigenetic changes already

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demonstrated in experimental animals, for example, in mice where it has been seen that MPs lead to an altered production and a completely different storage of lipids, to the modification in the synthesis of many proteins fundamental for neurological development, to the change of oxidation-reduction reactions and the production of acid radicals. All this taken as a whole and what can be called a "perfect storm" will bring about a change in the expression of diseases even in adulthood (12)

All the babies in whose placentas we found microplastics were healthy at birth. However potentially, MP/NPs, and in general microparticles, may alter several cellular regulating pathways in placenta, such as immunity mechanisms. The presence of MP/NPs in the placenta tissue requires the reconsideration of the immunological mechanism of self-tolerance, a mechanism that may be perturbed by the presence of MP/NPs. In fact, it is reported that, once present in the human body, MP/NPs may accumulate and exert localized toxicity by inducing and/or enhancing immune responses. This could potentially reduce the defense mechanisms against pathogens and alter the utilization of energy stores. So, it is likely that the presence of MP/NPs can change the ways in which the body, even of an adult, manages fat metabolism, likely through epigenetic modifications. (13).

Science need time…We make an analogy with what we know about smoking. We all know that smoking is dangerous and causes the onset of numerous cardiovascular and cerebral diseases, as well as lung cancers. However, to prove this simply fact it took more than forty years of medical research. There are three reasons for this. The first because research needs time, you have to prove whatever you affirm with evidence: this is one of the most important advantages of the scientific method, but on the other hand it is time consuming. A second problem is that the major companies, in this case tobacco producers, opposed and concealed for years the knowledge available with the enormous economic and financial means at their disposal. Similarly, right now we observe a big attempt at mystification by plastic companies, with respect to the evidence that is emerging on human health. Thirdly, since there is a 20-30 years' time-interval between the beginning of tobacco consumption and the onset of diseases it is not easy for human beings, for cognitive and social reasons, to precisely correlate a current action/behavior with what will happen in the future. The same happens with plastics and microplastics because they exert a toxic action not only immediately, but also diluted over time.

Recently, Amereh F. et al studied 43 pregnant women from general population, and their placentas were analyzed by digital microscopy and Raman microspectroscopy for microplastics (MPs <5 mm). They used regression analysis to estimate associations between MPs count in placenta and neonatal anthropometric measurements. MPs were found in all (13 out of 13) intrauterine growth restriction (IUGR) pregnancies and their average abundance ranged from 2 to 38 particles per placenta, but were below limit of detection in normal pregnancies except three out of 30 subjects. Inverse associations between MPs exposure and birth outcomes were observed in terms of birth weight, length, head circumference, and one-minute Apgar score among IUGR neonates, compared to those coming from normal pregnancies *(14).*

The babies we examined were all healthy, but it is important to note that we had examined healthy babies from normal pregnancies, while Amereh F. et al focused-on babies who were already small in utero. The result of his study, if confirmed, would be dramatically important, as it accounts for an effect of MPs that already occurs in utero.

The morphological alterations found in the placental cells could be the result of a prolonged attempt to remove and destroy the plastic particles inside the placental tissue. Continuous prolonged enzymatic decommissioning leads to an accumulation of toxic substances, with a subsequent persistent state of cellular alarm (CDR) that causes fetal phenotypic alterations in the long-term. The issue, however, is not "just" plastic. Chemicals in plastic products, such as phthalates and bisphenol A (BPA), act as endocrine disruptors. In children, who are still growing and developing, this can represent a big issue for the future.

We have discovered and described the presence of microplastics in human milk (15), but despite the presence of MPs in human milk, it remains the best food for newborns, in fact an abundant presence of microplastics has been demonstrated in baby formula.

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Microplastics were widely found in milk powder, and boxed formula powder has more plastic pollution than canned formula powder. The boxed baby formula powder mostly had inner linings made of polyethylene plastic and aluminum foil (16).

Use of commercially available single-use breastmilk storage bags determine ingestion by infants of microplastics and other particles, ingested by infants from the use of breastmilk storage bags. The quantity was estimated to be 0.61-0.89 mg/day based on the average daily breastmilk intake by infants. In addition, microplastic exposure from feeding bottles is 6.8 times higher than that from milk powder and milk powder preparation is 1.7 times higher.

More babies-focused research has estimated that a single baby's intake of microplastics from bottles is between 14,600 and 4,550,000 particles/day, with the lowest levels observed in Africa and Asia (16) This huge range highlights the great uncertainty about human exposure to MP/NPs, particularly in the first years of life, and the considerable analytical challenges of quantifying MP/NPs (17) showed that when shaken with hot water, plastic bottles release up to 16 million microplastics per liter and that sterilization and high-temperature water significantly increased the release of microplastics. Overall, they concluded that babies fed plastic bottles will be exposed to 14,600-4,550,000 particles/day.

Ultimately, the milk contained in these artificial containers is much richer in microplastics than breast milk and does not even have the same healthy characteristics as breast milk, for example all antibodies, for which women must be absolutely advised against using this type of artificial milk, unless it is absolutely necessary, despite the presence of microplastics, breast milk remains the ideal food for newborns. (18)

Breastfeeding should always be encouraged, and birthing places should continually improve their ability to advise women to breastfeed their newborns. Both cultural and architectural structures of birthplaces must be built with breastfeeding in mind. As we have explained succinctly, the benefits of breast milk, both for the mother and for the newborn, far outweigh the hypothetical health danger posed by the presence of MP/NPs.

Some benefits of breast milk are listed well on the CDC website: (19)

1. **"Breast milk is the best source of nutrition for most babies.**
   As the baby grows, the mother's breast milk will change to meet the baby's nutritional needs.
2. **Breastfeeding can help protect babies against some short- and long-term illnesses and diseases.**
   Breastfed babies have a lower risk of asthma, obesity, type 1 diabetes, and sudden infant death syndrome (SIDS). Breastfed babies are also less likely to have ear infections and stomach bugs.
3. **Breast milk shares antibodies from the mother with her baby.**
   These antibodies help babies develop a strong immune system and protect them from illnesses.
4. **Mothers can breastfeed anytime and anywhere.**
   Mothers can feed their babies on the go without worrying about having to mix formula or prepare bottles. When traveling, breastfeeding can also provide a source of comfort for babies whose normal routine is disrupted.
5. **Breastfeeding can reduce the mother's risk of breast and ovarian cancer, type 2 diabetes, and high blood pressure.**
   Breastfeeding has health benefits for the mother too! Some cancers, type 2 diabetes, and high blood pressure are less common among women who breastfeed.

The American Academy of Pediatrics recommends exclusive breastfeeding for about 6 months, and then continuing breastfeeding while introducing complementary foods until a child is 12 months old or older (20).

The solutions

We can all reduce plastic waste by reusing and recycling plastic, not buying, where possible, plastic objects of dubious utility and replacing them with others made from recyclable materials, not using water bottles and carbonated plastic drinks and plastic bags to do our daily shopping, do not

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use cosmetics that contain MP/NPs, use wooden toothbrushes and toothbrushes without MP/NPs, do not heat food in the microwave having placed it in plastic containers, even those officially authorized for this use actually dispose of large amounts of micro and nanoplastics in food, and so on. We can all use alternatives to plastic: fabric shopping bags, biodegradable plastic bags, jute bags, metal straws and non-plastic cutlery. Almost half (44.8%) of plastic polymer production is used for packaging, we can all support local companies that promote an ecological approach to the production and trade of their products and disadvantage companies that do not use this approach, filling our packages with unnecessary plastic. Finally, we must be aware that we will not solve the problem of plastic simply by using ingenious contraptions to clean up the seas, oceans, rivers and territories polluted by plastic. Although this may be commendable, new plastic will come and replace the old plastic that we have removed and secondly, we cannot think of treating our seas as if they were simply a garbage bin, to be filled and emptied, we must enter the realm of complexity.

But it will not be individual choices that will save us from a "plastic death" although they can be an example of virtuous behavior and positively "infect" others.

Not even recycling, a virtuous and useful behavior indeed, will save the planet (today less than 9% of the plastic produced is recycled). Although these virtuous individual behaviors are important and can represent a useful example, they are not enough to solve the problem represented by the 368 million tons of plastic produced just in 2019. This is why the action of enlightened governments, expression of voters aware of the political priorities of the planet, which are committed to change and reduce plastic production, is essential. Plastic has gradually replaced everything over the past sixty years, now it's time to replace it in turn. It is absolutely necessary to reduce the production of plastic, but this is not what is happening. The recent crisis caused by Covid, has meant that the major world petrochemical companies, especially from US and China have reconverted their fuel production systems, increasing the production of "virgin" plastic. China's plastics industry experienced a steady development in the first three quarters of the current year, with aggregate supplier revenues increasing 16.5% year-on-year. The aggregate operating revenues of plastic products manufacturers exceeded 1.58 trillion yuan (about $246.6 billion) in the January-September period. These companies collected total profits of 87.1 billion yuan, up 3.3% from a year earlier. In the first three quarters, China's plastics sector totaled production of 58.81 million tons, up 9.3% from the previous year (21).

Companies that produce and use plastic should be forced to deal with the end that objects will do next, once they must be disposed of, as it is done with spent batteries, where the cost of disposal is borne by the manufacturer. According to this environmental policy approach, a producer's responsibility should be extended to the post-consumer phase of a product's life cycle, unlike what is currently the case. In practice, it is inconceivable that companies produce goods at full capacity, which are put into circulation in the common environment, our Earth, without bearing the environmental costs of recycling or disposing of these same goods. On the contrary, they should be rigidly included in the production costs of the object, leading to a virtuous adjustment of market prices, which would allow plastic to be replaced with more environmentally convenient materials.

Extended producer responsibility is therefore a public policy instrument, whereby producers are legally and financially responsible for mitigating the environmental impact of their products. Let's take a simple hypothetical example: My company produces plastic cups, each costing 10 cents. Considering that paper ones would cost 15 cents each, it is clear that on the market the price of the plastic cup will be winning, and the consumer will not buy the paper cup for five cents more unless he is "rich" and motivated to do so. But if the cost of disposing of the plastic cup in the environment were borne by the producer, then that cup would cost 15 cents and not 10 and the producer would have to put it on the market at the same price as the paper cup. At this point, the buyer, for the same price, may find it more convenient to take home a paper cup.

The ban on unnecessary and single-use plastics combined with the obligation to pass on disposal costs to producers (as is done with spent batteries) and deeper systemic changes, aimed at a fully circular economy, would lead to reducing the amount of plastic that ends up in the oceans by up to 80% in the next 20 years. This is no small achievement.

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The so-called performative environmentalism, the one that has to do with daily and individual actions should therefore not be underestimated, because in fact it allows us to exercise our power to change and direct personal behaviors towards more sustainable and environmentally friendly choices. However, these are still individual actions, which do not change the logic of the global market. We can also no longer buy plastic straws or SUVs, choose to travel by bicycle and not by car, to travel by train and not by plane, to be vegetarians and not carnivores: these are all choices certainly dictated by positive intentions. The point is that they do not necessarily question the power structures within multinationals and governments, general or local. The risk is that by focusing on individual choices, people move away from the public sphere, confine themselves into the private and stop promoting the bonds that transform people into a community, that is, into a group of citizens able to elect and subsequently direct those who govern them in the interest of the common good and the environment in general. A group that acts collectively, in short, with the aim of delivering the Earth to those who will come after us in better conditions than those in which we received it. For this to be possible, however, it is essential that the political awareness matures that resources are not infinite and that we cannot do with the planet what we want.

We need what Pope Francis calls an "ecological conversion." Unfortunately, and here lies the greatest difficulty, "conversion" must be subjective and not only objective, but it must also concern the subjective element of the modification of our personal lifestyles, not only the objective element of the modification of the productive structures of local and planetary government systems. In other words, we absolutely need conscious citizens to elect politicians who can lead change. Nothing to say therefore about individual ecological choices, but we cannot ignore the choices of global politics.

The initial decalogue to address the problem could be the following:

1. Sign international agreements to reduce the production of "virgin" plastic.
2. Shoulder the responsibility and costs of plastic producers for its disposal.
3. Gradually replace plastic with recyclable material of natural origin.
4. Increase the recycling rate of plastic materials.
5. Ban the sale of mineral water and carbonated soft drinks in plastic containers and abolish the use and production of single-use plastics (straws, bags, plates, cutlery and plastic cups).
6. Use organic materials for packaging.
7. Produce natural plastic with algae, potatoes and corn, etc.
8. Buy bulk and non-plastic packaged foods.
9. Buy clothing made from natural and non-synthetic materials.
10. Teach all this in schools (22)

Conclusion

More than 55% of the plastic produced and thrown away in the world is produced by less than 20 companies (23) 20 companies that have stratospheric incomes and issue invoices, which we will all pay: eight billion individuals, mostly unaware of what is happening. Can we continue to sacrifice the good of the many for the profit of the few? (24).

In the opinion of Norbert Wiener, pioneer of cybernetics, it is human flexibility and communicative integrity that are violated and paralyzed by the current tendency of technology to subordinate man to his needs and his incessant progress.

Within a system based on technology and on the continuous creation of new machines, the individual should recover his own humanity in the relationship with technical tools, developing the potential that is proper to him: "We must cultivate the fertility of thought as we have cultivated the efficiency of administration. [...] We must not reduce ourselves to the condition of slaves, registered as property in the registers of our entrepreneurs. We need to create a system in which adaptability and variability are a function of improvement. We need an organization that is attentive to new inventions and our ever-increasing need for new inventions. If man is to continue to exist, he must no longer be considered less important than business. "[The Human Use Of Human Beings: Cybernetics And Society, Norbert Wiener (25).

Camus argued in the essay “The Man in Revolt” that: "to be, man must rebel". Only in this way is it possible to give meaning to one's existence, the reason for the revolt is: "... In wanting to serve justice so as not to increase the injustice of the human condition, in striving for clear language so as not to thicken the universal lie and in focusing, despite human misery, on happiness".

Unfortunately, the ability of some pollutants to be transferred from mother to baby through breastfeeding is well known. Pollutants such as heat treatment chemicals, pesticides, toxins, packaging material residues and metals/metalloids, among others, can appear in both breast milk and infant formula (26).

Different MPs, with different concentrations have been found also in:

Blood: from pigs and cows;

Milk: from cows including hand-milked milk, tank milk, and packaged milk from supermarkets;

Feed: feed pellets, fresh feed roughage, and shredded supermarket feed;

Meat: meat samples, all plastic-packaged, including filet and processed meat products (from both farms and supermarkets) (27)

In essence, the composition of breast milk reflects with a certain approximation the degree of pollution of the place that women/animals live in as well as their habits of life. However, salvation from these toxic products cannot be contained in the infant formula that in addition to containing pollutants in turn does not have the health-stimulating properties that breast milk has. Salvation should be found in protecting the environment to pour less pollutants, especially when they are not biodegradable in the surrounding environment. Ultimately, we need politicians with greater sensitivity to the problem and to do this naturally we should start with voters who know how to choose politicians with greater sensitivity.

Author Contributions: All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Conflict of Interest: The authors declare that the present review paper was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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