Commentary

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Microplastic exposure is associated with male reproductive health

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Background

Over the past few decades, the insidious proliferation of plastic contaminants has emerged as a pervasive environmental challenge, with far-reaching implications for the integrity of oceans and a myriad of natural ecosystems, even looming as a significant risk [1] to human health. Plastics subjected to environmental degradation undergo an intricate transformation process, fragmenting into microplastics (MPs) that are disseminated and translocated across global environments such as oceans, lakes, rivers and soils. These MPs, defined by their diminutive size of less than 5 mm, are particularly concerning due to their propensity to infiltrate the food chain. The ingestion of such particles introduces potential hazards to human health, as evidenced by the increasing detection of MPs in various consumables. Human exposure to MPs is facilitated through multiple exposure pathways, including the consumption of food [2], ingestion of water [3] and inhalation of air [4]. The food chain is increasingly recognized as a principal conduit for the entry of MPs into the human body, with these particles now being identified in a vast array of foodstuffs, ranging from seafood to bottled water, milk, beer, and even table salt [5, 6]. Moreover, the pervasive presence of MPs extends to key organ systems within the human body, affecting the digestive, respiratory, circulatory [7], reproductive, nervous, immune, endocrine, urinary, and locomotor systems [2, 8].

Microplastic exposure is associated with male reproductive health

With respect to the global landscape of reproductive health, more than 186 million individuals are afflicted by infertility [9]; with a substantial proportion, more than half of cases suffer from male infertility [10]. Despite the advancement of assisted reproductive technologies, these methods have not consistently translated into an appreciable increase in live birth rates [11]. In light of these statistics, the significance of focusing on the health of the male reproductive system cannot be overlooked. Although no direct relationships between MP contamination and human reproductive health have been established to date, the impact of environmental contaminants, particularly particulate matter, on human health outcomes has been well documented [12–14]. This evidence underscores the need for a vigilant

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examination of all potential factors that may contribute to the decline in male reproductive health, including the possible role of MPs.

The global surge in plastic production, particularly in China, over the past half-century (1970s–2020s) has been juxtaposed with a stark decline in the semen quality of donors, precipitously plummeting post-2010 to the present [15–17] (Figure 1), which reveals a disconcerting inverse relationship where the burgeoning plastics industry has flourished in tandem with a retreat from optimal male reproductive health. Moreover, in these 50 years, the proliferation of plastic products and their subsequent disposal into the environment have resulted in the pervasive breakdown of plastic products into MPs, which have been found to be involved in numerous pathways in the human body, traversing the blood-testis barrier and infiltrating the reproductive system [15, 18]. This infiltration of MPs into the reproductive sphere poses a significant threat to fertility and the overall health of future generations. In addition, the decline in birth rates within major economies around the world is heralding an era of population aging, which has profound implications for socioeconomic stability and growth. As such, the interplay between plastic pollution and reproductive health has emerged not only as a public health concern but also as a critical issue with far-reaching socioeconomic ramifications.

Semen analysis is an indispensable element in the comprehensive evaluation of infertility [19], providing critical insights into the state of male reproductive health. It is evident that a multitude of factors contribute to the observed decline in male fertility; however, the potential impact of MPs on reproductive capabilities warrants serious consideration, and the correlation between MPs and male infertility cannot be ignored [20]. To the best of our knowledge, we propose a novel hypothesis positing an association between MPs and male reproductive health. Although a direct causal link has yet to be established, compelling evidence suggests that the chronic toxic effects of MPs may pose a significant threat to the vitality of the male reproductive system, while this hypothesis opens a new avenue for research, inviting further investigation into the mechanisms by which MPs might adversely influence fertility and reproductive well-being.

At present, there have been reports of male reproductive harm or impairment associated with exposure to MPs. The composition of MPs is complex, comprising not only primary plastic constituents such as polyethene, polypropylene, polystyrene, and polyvinyl chloride but also a variety of chemical additives, including phthalates and bisphenols. These additives are ubiquitously employed in the manufacturing of plastic products, including food containers, water bottles, and toys [21].

The principal detrimental effects observed are manifold and include (a) reproductive dysfunction, which can manifest in various ways and impact overall reproductive capacity [22]; (b) alterations in biochemical, spermatogenic, and histological parameters, which might reflect disturbances in the intricate processes underlying sperm production and male reproductive health [23]; (c) diminished levels of testosterone, a critical hormone for maintaining male reproductive functions and secondary sexual characteristics [24]; and (d) the induction of oxidative stress and inflammatory responses, which can lead to a cascade of negative effects on sperm quality and testicular health [25]. These adverse outcomes have the potential to compromise male reproductive fitness and may, in turn, significantly influence fertility rates. Understanding the mechanistic links between MPs and these adverse effects is essential

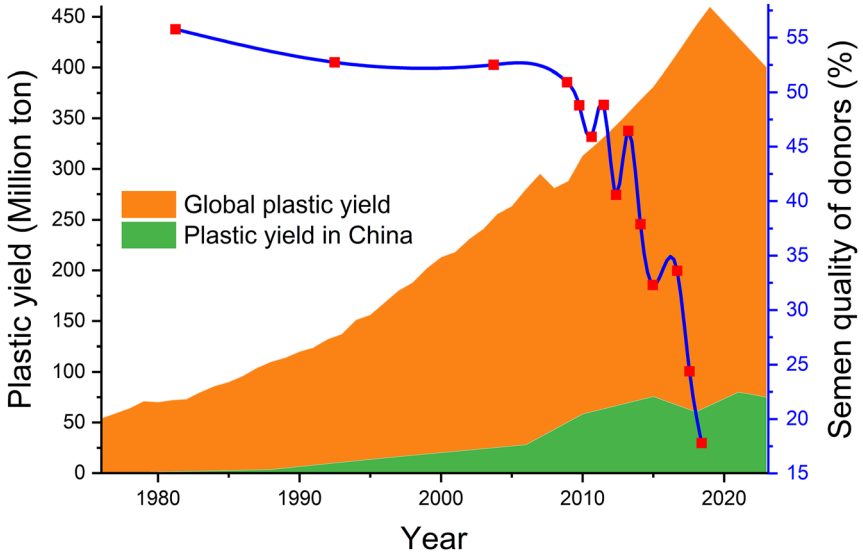

Figure 1: Trends in plastic yield and semen quality of donors in the 1970s–2020s. Data source: The annual plastic production trend of global (https://ourworldindata.org/grapher/global-plastics-production#research-and-writing) and China (https://bg.qianzhan.com/report/detail/76d7518878 8c4f34.html). Semen quality of donors in the 1970s–2020s: https://doi.org/10.1007/s10815-023-02859-z.

for developing preventive measures and therapeutic interventions aimed at preserving and enhancing male reproductive health.

Elucidating the association between MP contamination and male reproductive health necessitates the amalgamation of cutting-edge technologies and innovative methodologies, including (a) environmental surveillance to quantify MP concentrations and evaluate dose-response relationships, thereby gauging the pervasiveness and toxicological impact of MPs within the environment over a defined period; (b) comprehensive analysis, such as differential gene expression, differential protein expression and differentially abundant metabolite expression, by systematic toxicology and integrated 'omics' techniques, which entails assessing semen quality, scrutinizing the integrity of the blood-testis barrier, quantifying MP levels in semen, identifying biomarkers indicative of damage, and examining multiomics alterations. It is also imperative to establish a robust framework of norms and standards for MP analysis in biological matrices; (c) investigating toxicological effects at both *in vivo* and *in vitro* levels in male animal models [26], which may yield valuable insights and corroborative evidence for understanding the health implications of MPs on the human male reproductive system; (d) exploring specific biomarkers [27], including proteins, DNA [28], RNA and small molecular metabolites, etc., for adverse effects on male reproductive health; and (d) synthesizing evidence from epidemiological studies and conducting prospective, multicenter, observational cohort These multidisciplinary approaches are pivotal in advancing our understanding and informing strategies to mitigate the impact of MPs on human health and the environment.

To date, the relationship between the burgeoning plastics industry and the observed decrease in male reproductive health presents a multifaceted challenge that defies straightforward resolution. Nonetheless, by recognizing the magnitude of this issue and implementing strategic interventions, there is potential to mitigate the prevailing negative trends. To effectively manage and curtail MP contamination and human exposure, a multipronged approach is advocated, which includes (a) curbing the consumption of plastic items and advocating for eco-friendly, sustainable alternatives to conventional plastics, alongside the enforcement of more stringent regulations on the utilization of deleterious chemicals in plastic manufacturing processes; (b) strengthening the global strategy [29] and bolstering international efforts to combat plastic contamination and enhance the recycling of plastic waste; (c) elevating public consciousness regarding the risks associated with MPs; and (d) conducting comprehensive research to more accurately assess the extent of health risks [30] and discern the mechanisms by which MPs may impair reproductive health. Such investigations have profound implications for global public health because of the increasing prevalence of male infertility across the globe.

In conclusion, the correlation between environmental MP exposure and implications for male reproductive health warrants further investigation and empirical substantiation. The identification and exploration of relevant biomarkers are pivotal, as they may help to elucidate the specific pathways by which MPs may exert adverse effects on male fertility. The ramifications of such research are profound, with the potential to inform public health strategies and environmental policies. Ultimately, it is imperative that a collaborative and concerted effort is undertaken to address the multifaceted challenges associated with the decline in male reproductive health and the pervasive influence of plastic contamination on our communities and the natural world. Through a shared commitment to responsible stewardship and collective action, we can envision and actualize a future that is both healthier for humankind and more sustainable for our planet, ensuring the well-being of current and future generations.

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