

Author's reply to comments on: Micro- and nanoplastics and the kidney: exposure pathways, toxicokinetics, and pathophysiological insights

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We thank Drs. Renda, Gallina, and Mattioli for their thoughtful comments on our article concerning micro- and nanoplastics (MNPs) and kidney health.

We fully agree that the biological effects of MNP exposure should be interpreted within a broader cardio-reno-metabolic framework. As highlighted by the authors, oxidative stress, chronic inflammation, endothelial dysfunction, metabolic alterations, and activation of neurohormonal pathways represent common mechanisms linking environmental exposure to cardiovascular, renal, and metabolic disease.

In this regard, the recently proposed cardio-kidney-metabolic (CKM) syndrome provides a particularly useful conceptual framework. The CKM model recognizes the complex bidirectional interactions linking metabolic dysfunction, cardiovascular disease, and kidney damage. Environmental stressors such as micro- and nanoplastics may represent an additional and still underappreciated upstream contributor capable of simultaneously affecting all three domains through shared mechanisms, including oxidative stress, inflammation, endothelial dysfunction, and metabolic dysregulation.

The emerging evidence demonstrating the presence of microplastics within atherosclerotic plaques and their

association with adverse cardiovascular outcomes further supports the concept that MNPs may act as systemic rather than organ-specific stressors.

From a nephrological perspective, we would also emphasize that the kidney may represent one of the earliest target organs of chronic environmental exposure. Owing to its high blood flow, filtration function, and tubular concentrating mechanisms, the kidney is continuously exposed to circulating contaminants and may therefore serve as a sensitive biological sentinel of environmental injury.

We also share the authors' view that climate change, environmental pollution, and cardio-reno-metabolic disease should increasingly be considered interconnected phenomena rather than separate entities. Integrating environmental determinants into preventive nephrology and cardiovascular medicine may become an important challenge for future research and public health strategies.

We are grateful to the authors for broadening the discussion and for emphasizing the potential relevance of MNPs within the evolving cardio-reno-metabolic paradigm.

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