

## Long-term exposure to volcanic ash deposits & health-related impacts

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Volcanic eruptions release a range of sizes of particles and can affect communities up to thousands of kilometers away from the volcano. Acute respiratory disorders have been documented in exposed populations and evidenced by *in-vivo* and *in-vitro* studies reporting adverse lung effects and enhanced inflammatory response induced by short-term exposure to fine (<10µm) volcanic ash. Volcanic activity can however be recurrent for long periods of time and volcanic ash resuspension can exacerbate the health impact of primary eruptive events from the time of deposition up to many years after an eruption. So far, our global understanding of the health effects triggered by long-term (i.e., chronic) exposure to volcanic particles through multiple pathways (inhalation and oral ingestion) and at the whole-body scale is extremely limited.

In a recent study [1], we demonstrated that mice exposed to metal-rich volcanic ash deposits presented an organ-specific and isotopically-typified metallome deregulation, associated with pronounced pathophysiological changes. These deregulations extended far beyond the pulmonary system and significantly impacted the testes as evidenced by spermatogenesis alteration.

To further answer whether chronic exposure can trigger development of fertility disorders, we extended the exposure of mice (C57BL/6) up to two months. Chemical analyses (major and trace element concentrations) and Cu-Zn-Fe isotope measurements coupled to proteomic and transcriptomic analyses were measured in 9 organs and 2 biological fluids, with a focus on testes. We found that heavy metal accumulation was still omnipresent in the testes after two months of exposure but significant copper and iron isotopic fractionations appear. These isotopic variations correlate with the downregulation of testicular glutathione peroxidase (GPX) gene expression and blood superoxide dismutase (SOD) activity. Aiming at scavenging harmful reactive oxygen species (ROS) and preventing ROS-induced oxidative stress, the reduced expression and/or loss of activity of these two main antioxidant enzymes suggests a greater vulnerability of the male reproductive system to oxidative stress. Altogether, these results demonstrate that prolonged exposure to metal-rich ash induces testicular toxicity and suggest that Cu-Fe isotopic compositions might help identifying early signs of oxidative stress that potentially exacerbate testicular defects over time exposure.

[1] Sauzéat et al., STE, 829, 154383 (2022)