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Evidence for a role of paternal exposures
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Despite high plausibility, impact of environmental exposures on alterations in the paternal genetic load and/or its transmission, resulting potentially in developmental abnormalities, is still not demonstrated in humans.

Experimental evidence from radiation exposure, antimitotic drugs such as cyclophosphamide, or chemicals such as pesticides or metals, does suggest the possibility of transmission of paternally-mediated developmental effects. The mechanistic framework for male-mediated developmental effects is growing with suggestion of transmission of epigenetic modifications as a possible mechanism, in addition to germ line mutagenesis. Unfortunately, if the experimental literature supports the plausibility of male-mediated effects in a general way, it does not make a strong mechanistic case for these exposures affecting specific outcomes.

The number and quality of epidemiological studies regarding effects of prevalent and well characterized paternal exposures such as tobacco smoke or ionizing radiation on intrauterine development is quite limited. Most studies have focused on birth defects and childhood cancers in association with occupational exposures. Overall, there is still no convincing evidence from this research. Endpoints such as miscarriage, birth weight, preterm birth and neurobehavioral parameters have been barely studied. Most studies have included paternal exposures as an add-on to existing studies and there are few if any studies in which the paternal role in development has been the primary focus of major research initiatives.

Improved knowledge on possible consequences of paternal exposures in future generations is needed and has strong implication in terms of regulation, in the workplace for instance. One may expect human studies to be conducted, specific to male-mediated developmental toxicity, developing and using biological markers pertinent to hypothesized mechanisms identified in animal studies.