

PARENTAL LOW DOSE EXPOSURE TO NITROSODIMETHYLAMINE CAN IMPACT SEXUAL DEVELOPMENT AND REPRODUCTIVE PARAMETERS OF MALE OFFSPRING IN RATS

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INTRODUCTION: N-Nitrosodimethylamine (NDMA) is a compound from the N-nitrosamine class, a residue of industrial processes. Its presence in drinking water, food, and medications has raised global regulatory concerns, as it is classified as a *Cohort of Concern* due to its mutagenic and carcinogenic potential. However, its impact on reproductive health, especially at low doses, remains poorly understood. **OBJECTIVE:** This study aimed to investigate the effects of indirect NDMA exposure - through maternal, paternal, and combined routes - on toxicological and reproductive parameters in F1 generation of male Wistar rats. **METHODS:** The F0 generation consisted of 40 male and 40 female Wistar rats allocated into four experimental groups (n=10/group/sex): Control (control males and females); Maternal NDMA (control males, NDMA-exposed females); Paternal NDMA (NDMA-exposed males, control females); and Combined NDMA (both sexes NDMA-exposed). Control animals received 1 ml/kg of distilled water, and NDMA groups received 7.2 ng/kg/day orally (by gavage) from postnatal day (PND) 60 to 90 and during mating, gestation, and lactation period. F1 offspring were evaluated for early sexual development and pubertal onset. On PND 70, they were euthanized for organ collection and Leydig cell histology. **RESULTS AND CONCLUSION:** No statistical differences were observed in body weight or absolute/relative anogenital distance on PND 1, 13 and 22. However, delayed testicular descent was noted in the Combined NDMA group, although no differences were found in preputial separation. On PND 70, an increase in the absolute weight of the full seminal vesicle was observed in the Paternal NDMA group. Additionally, increased nuclear area, volume, and number of Leydig cells were found in this group. In conclusion, NDMA exposure, particularly through the paternal route, affected parameters associated with androgenic hormonal regulation. As Leydig cells play a key role in testosterone production and sexual development, these findings suggest that low-dose NDMA exposure may influence reproductive health in offspring.

Keywords: reproductive toxicology; male fertility; pollutants; nitrosamines.

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