EDC IMPACT: Reduced sperm counts in rats exposed to human relevant mixtures of endocrine disrupters

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Human semen quality is declining in many parts of the world, but the causes are ill defined. In rodents, impaired sperm production can be seen with early life exposure to certain endocrine-disrupting chemicals, but the effects of combined exposures are not properly investigated. In this study, we examined the effects of early exposure to the painkiller paracetamol and mixtures of human relevant endocrine-disrupting chemicals in rats. One mixture contained four estrogenic compounds; another contained eight anti-androgenic environmental chemicals and a third mixture contained estrogens, anti-androgens and paracetamol. All exposures were administered by oral gavage to time-mated Wistar dams rats (n=16-20) throughout gestation and lactation. In the postnatal period, testicular histology was affected by the total mixture, and at the end of weaning, male testis weights were significantly increased by paracetamol and the high doses of the total and the anti-androgenic mixture, compared to controls. In all dose groups, epididymal sperm counts were reduced several months after end of exposure, i.e. at 10 months of age. Interestingly, the same pattern of effects was seen for paracetamol as for mixtures with diverse modes of action. Reduced sperm count was seen at a dose level reflecting human therapeutic exposure to paracetamol. Environmental chemical mixtures affected sperm count at the lowest mixture dose indicating an insufficient margin of safety for the most exposed humans. This causes concern for exposure of pregnant women to paracetamol as well as environmental endocrine disrupters.