Disinfectant Exposure Decreases Reproductive Hormones

BACKGROUND

ADBAC (alkyldimethylbenzyl ammonium chloride) and DDAC (didecyldimethyl ammonium chloride) are two quaternary ammonium compounds. ADBAC and DDAC are common in household cleaners, personal care products, inks, paints, and makeup. Recent studies by our lab found that chronic exposure decreased reproduction in male and female mice.¹⁻² Others have found that exposure inhibits mitochondrial function, cholesterol synthesis and causes blockade of the estrogen receptor. Reproductive function is directed by follicle stimulating hormone (FSH) and luteinizing hormone (LH). Both are regulated by estrogen via the hypothalamic-pituitary-gonadal axis.

HYPOTHESIS

We hypothesized that ADBAC+DDAC exposure would alter FSH and LH production in both ambiently exposed and dosed mice

Ambient mice are not experimentally dosed, but receive exposure from normal use of disinfectant in the mouse room

MATERIALS and METHODS

- Three treatment groups of CD-1 mice
 - Unexposed controls
 - Ambient exposure through normal use of disinfectant
 - \circ Dosed exposure (60 mg/kg/day in the feed + ambient)
- F0 parents exposed
 - 10 days prior to breeding
 - Through out gestation and lactation
- F1 Pups born to exposed F0 parents
 - Exposed during gestation and lactation
 - Exposure ceased at 21 days old
- F1 pups bled at 40 days of age (8 male, 8 female/group)
- FSH and LH determined by ELISA (Abnova)

Age	50	60	70	80	90	100	110			
			/0	00	50	100	110			
F0	Dose	Breed	Ge	estate	Lactate		_ [20	30	40
	F1 Born Wean									
										\vee
Blood										
QAC Dose V Collected Age (days)										

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Terry C. Hrubec^{1,2}, Pamela Vieira¹, Valerie A. McDonald¹

¹E. Via College of Osteopathic Medicine, Virginia Campus, Blacksburg, VA ²VA-MD College of Veterinary Medicine, Virginia Tech, Blacksburg, VA









FSH and LH are decreased in mice exposed to ADBAC+DDAC

Different letters above bars denotes significant differences between groups by ANOVA $p \le 0.05$ N = 8 per treatment group, dosed mice received 60 mg/kg

Ambient







Hypothalamicpituitary-gonadal-axis (HPGA) feedback loop GnRH, produced in the hypothalamus of the brain, acts on the pituitary gland to produce FSH and LH. These in turn act on the ovaries or testes to produce estrogen and testosterone which then provide feedback to the brain to regulate GnRH.

FSH Stimulates follicle development in the ovary (females) Increases estrogen (females) Stimulates sperm production (males) Increases testosterone (males) LH Stimulates estrogen production (females) Controls the menstrual cycle (females) **Triggers ovulation (females)** Sustains production of progesterone and thus pregnancy Stimulates testosterone production (males) Accentuates male characteristics - muscle mass, facial hair, etc. (males)

CONCLUSIONS

- **Early life exposure to ADBAC+DDAC reduced FSH and LH**
- Both hormones were reduced indicating direct action on GnRH production or blockade of the estrogen receptor
- **ADBAC+DDAC** disrupt endocrine function even with ambient use
- Reduced FSH and LH likely cause the declines in male and female fertility

ONE HEALTH CONCERNS

- **Exposure to quaternary ammonium compounds is extensive**
- Most HPGA endocrine disruptors also disrupt growth hormone, thyroid hormones, and ACTH
- Human infertility has increased over the last 20 years in part from environmental factors. ADBAC+DDAC exposure may be contributing to this increase in infertility

Acknowledgements - Citations

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1. Melin VE, et al., 2014. Exposure to common quaternary ammonium disinfectants decreases fertility in mice. Reproductive Toxicology. http://dx.doi.org/10.1016/j.reprotox.2014.07.071 2. Melin VE, et al., 2015. Quaternary ammonium disinfectants cause subfertility in mice by targeting both male and female reproductive processes. Reproductive Toxicology. http://dx.doi.org/10.1016 /j.reprotox.2015.10.006 3. Datta S, et al., 2017. In vitro evaluation of mitochondrial function and estrogen signaling in cell lines exposed to the antiseptic cetylpyridinium chloride. Environ Health Perspect. 125: 087015.