## HALTING THE INERTIA OF INDIFFERENCE: FLUORIDE AND FERTILITY REVISITED

SUMMARY: Two new studies have demonstrated that fluoride can impair male fertility. The first, in mice, found fluoride decreases sperm hyperactivation and Catsper1 gene expression. The second, in rats, reports that fluoride decreases sperm motility, enhances oxidative stress in testis, and increases testis apoptosis. These findings are consistent with many earlier reports of adverse fluoride effects, including some of reduced fertility in animals drinking water containing 1 ppm of fluoride. The current recommendation by some authorities for adding fluoride to community water supplies is likely to impair male fertility.

Keywords: Fertility; Fluoridation; Indifference to fluoride effects on fertility; Infertility; Mice; Rats; Spermatozoal hypermotility; Spermatozoal motility; Testis apoptosis; Testis oxidative stress.

Two further articles on the adverse effects of fluoride on male reproductive function are included in the present issue. Wang et al. found that fluoride in mice decreases sperm hyperactivation and Catsper1 gene expression.<sup>1</sup> Zhang et al. report that fluoride in rats decreases sperm motility, enhances oxidative stress in testis, and increases testis apoptosis.<sup>2</sup> These studies follow many previous reports published in *Fluoride* and other peer-reviewed publications of the detrimental effects of fluoride on male reproductive function.<sup>3-34</sup>

The need for additional studies of a possible association between fluoride and reproductive parameters was noted in a chapter on "Reproductive and developmental effects of fluoride" in the 2006 National Research Council publication *Fluoride in drinking water: a scientific review of EPA's standards* notes.<sup>35</sup> The two new studies now reported provide examples of such information as suggested. These findings are consistent with many earlier reports of fluoride adverse effects, including some of reduced fertility in animals drinking water containing 1 ppm of fluoride.<sup>36-40</sup>

Currently the authorities who recommend adding fluoride at 0.7–1.2 ppm to community water supplies give little attention to the effect of fluoride on male fertility. For example, the 2007 Australian Government publication *A systematic review of the efficacy and safety of fluoridation* found that the existing body of evidence strongly suggested that water fluoridation is beneficial at reducing dental caries but did not discuss the concerns about the effects of fluoride on fertility.<sup>41</sup>

Adding fluoride to community water supplies is likely to impair male fertility. The two studies reported in this issue provide further friction to help halt this inertia of indifference to the adverse effects of fluoride on male reproductive function.

> Bruce Spittle MB ChB DPM FRANZCP, Managing Editor, *Fluoride* 727 Brighton Road, Ocean View Dunedin 9035, New Zealand

## REFERENCES

- 1 Sun ZL, Wang B, Niu RY, Zhang JH, Wang JD. Decreased sperm hyperactivation and low Catsper1 expression in mice exposed to fluoride. Fluoride 2009;42(3):167-173.
- 2 Wang JL, Zhang YM, Zhang HJ, Zhang K, Zhang ZW, Li J. Toxic effects of fluoride on reproductive ability in male rats: sperm motility, oxidative stress, cell cycle, and testicular apoptosis. Fluoride 2009;42(3): 174-178.
- 3 Spittle B. Fluoride and fertility [editorial]. Fluoride 2008;41(2):98-100.
- 4 Kour K, Singh J. Histological finding of mice testes following fluoride ingestion. Fluoride 1980;13(4):160-2.
- 5 Zahvoronkov AA, Strochkova LS. Fluorosis: geographical pathology and some experimental findings. Fluoride 1981;14(4):182-91.
- 6 Mehdi AWR, Al-Soudi KA, Al-Jiboori NAJ, Al-Hiti MK. Effect of high fluoride intake on chicken performance, ovulation, spermatogenesis and bone fluoride content. Fluoride1983;16(1):37-43.
- 7 Mandrik FI, Yakubovskaya YuL. Gonado-embrotoxicity of fluorine. Veterinariya 1984;11:66-7.[in Russian, abstract in Fluoride 1986;19(3):154].
- 8 Chinoy NJ, Sequeira E. Fluoride induced biochemical changes in reproductive organs of male mice. Fluoride1989;22(2):78-85.
- 9 Chinoy NJ, Sequeira E, Narayana MV. Effects of vitamin C and calcium on the reversibility of fluoride-induced alternations in spermatozoa of rabbits. Fluoride 1991;24(1):29-39.
- 10 Chinoy NJ, Sequeira E. Reversible fluoride induced fertility impairment in male mice. Fluoride 1992;25(2):71-6.
- 11 Susheela AK, Kumar A. A study of the effects of high concentrations of fluoride on the reproductive organs of male rabbits, using light and scanning electron microscopy. J Reprod Fertil 1991;92(2):353-60.[abstract in Fluoride 1993;26(2):148].
- 12 Narayana MV, Chinoy NJ. Effect of fluoride on rat testicular steroidogenesis. Fluoride 1994;27(1):7-12.
- 13 Chinoy NJ, Reddy VVPC, Michael M. Beneficial effects of ascorbic acid and calcium on reproductive functions of sodium fluoride-treated prepubertal male rats. Fluoride 1994;27(2):67-75.
- 14 Freni SC. Exposure to high fluoride concentrations in drinking water is associated with decreased birth rates. J Toxicol Environ Health 1994;42(1):109-21.[abstract in Fluoride1994;27(4):231].
- 15 Chinoy NJ, Narayana MV. *In vitro* fluoride toxicity in human spermatozoa. Reprod Toxicol 1994;8(2):155-9. [abstract in Fluoride 1994;27(4):231-2 and Fluoride 1995;28(1):48-9].
- 16 Kumar A, Susheela AK. Ultrastructural studies of spermiogenesis in rabbit exposed to chronic fluoride toxicity. Int J Fertil Menopausal Stud 1994;39(3):161-71 [abstract in Fluoride 1995;28(1):49.
- 17 Chinoy NJ, Narayana MV, Dalal V, Rawat M, Patel D. Amelioration of fluoride toxicity in some accessory reproductive glands and spermatozoa of rat. Fluoride 1995;28(2):75-86.
- 18 Narayana MV, Chinoy NJ. Reversible effects of sodium fluoride ingestion on spermatozoa of the rat. Int J Fertil Menopausal Stud 1994;39(6):337-46. [abstract in Fluoride 1995;28(3):150].
- 19 Kumar A, Susheela AK. Effects of chronic fluoride toxicity on the morphology of ductus epididymis and the maturation of spermatozoa of rabbit. Int J Exp Pathol1995;76(1):1-11. [abstract in Fluoride 1995;28(3):151].
- 20 Sprando RL, Black TN, Ames MJ, Rorie JI, Collins TFX. Effect of intratesticular injection of sodium fluoride on spermatogenesis. Food Chem Toxicol 1996;34(4):377-84. [abstract in Fluoride 1996;29(3):182].
- 21 Krasowska A, Wlostowski T. Photoperiodic elevation of testicular zinc protects seminferous tubules against fluoride toxicity in the bank vole (*Clethrionomys glareolus*). Comp Biochem Physiol C Pharmacol Toxicol 1996;113(1):81-4. [abstract in Fluoride 1996;29(3):183-4].
- 22 Susheela AK, Jethanandani P. Circulating testosterone levels in skeletal fluorosis patients. J Toxicol Clin Toxicol 1996;34(2):183-9.

- 161 Editorial Fluoride 42(3)159–161 July-September 2009
- 23 Sprando RL, Collins TFX, Black TN, Rorie JI, Ames MJ, O'Donnell M. Testing the potential of sodium fluoride to affect spermatogenesis in the rat. Food Chem Toxicol 1997;35(9):881-90. [abstract in Fluoride 1998;31(1):49].
- 24 Chinoy NJ, Sharma A. Reversal of fluoride-induced alterations of cauda epididymal spermatozoa and fertility impairment in male mice. Fluoride 1998;31(3):S26 [abstract].
- 25 Chinoy NJ, Sharma A. Amelioration of fluoride toxicity by vitamins E and D in reproductive functions of male mice. Fluoride 1998;31(4);203-16.
- 26 Bhatnagar M, Susheela AK, Soundaram CC, Takkar D. Effect of fluoride contamination of drinking water on human spermatozoa. Fluoride 2001;34(3):196 [abstract].
- 27 Zakrzewska H, Udała J, Błaszczyk B. *In vitro* influence of sodium fluoride on ram semen quality and enzyme activities. Fluoride 2002;35(3):153-60.
- 28 Ortiz-Pérez D, Rodriquez-Martínez M, Martínez F, Boria-Aburto VH, Castelo J, Grimaldo JI, et al. Fluoride-induced disruption of reproductive hormones in men. Environ Res 2003;93(1):20-30.
- 29 Zhang JH, Liang C, Ma JJ, Niu RY, Wang JD. Effects of sodium fluoride and sulfur dioxide on sperm motility and serum testosterone in male rats. Fluoride 2006;39(2):126-31.
- 30 Huang C, Nui RY, Wang JD. Toxic effects of sodium fluoride on reproductive function in male mice. Fluoride 2007;40(3):162-8.
- 31 Ma XY, Gao LH, Hou J, Cui LX. Study of reproductive endocrine disturbances in fluoride exposed population [abstract]. Fluoride 2007;40(4):261.
- 32 Sundaram C. The effects of fluoride contamination of drinking water on human semen status and sperm ultra structure [thesis]. New Delhi, India: All India Institute of Medical Sciences; 1998. Cited in: Susheela AK. A treatise on fluorosis. 3rd ed. Delhi, India: Fluorosis Research and Rural Development Foundation; 2007. p. 54-5.
- 33 Huang C, Yang HB, Niu RY, Sun ZL, Wang JD. Effects of sodium fluoride on androgen receptor expression in male mice. Fluoride 2008;41(1):10-17.
- 34 Izquierdo-Vega JA, Sánchez-Gutiérrez M, Del Razo LM. Decreased *in vitro* fertility in male rats exposed to fluoride-induced oxidative stress damage and mitochondrial transmembrane potential loss. Toxicol Appl Pharmacol 2008;230(3):352-7. Epub 2008 Mar 28. [abstract in Fluoride 2008;41(2):171-2].
- 35 Doull J, Boekelheide K, Farishian BG, Isaacson RL, Klotz JB, Kumar JV, Limeback H, Poole C, Puzas JE, Reed N-MR, Thiessen KM, Webster TF, Committee on Fluoride in Drinking Water, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies, National Research Council of the National Academies. Fluoride in drinking water: a scientific review of EPA's standards. Washington, DC: The National Academies Press; 2006. p.181-204. [Contract No.: 68-C-03-013. Sponsored by the U.S. Environmental Protection Agency]. Available to read or purchase on line at www.nap.edu.
- 36 Cox WR. Hello test animals ... chinchillas? or you and your grandchildren. Milwaukee, WI: Lee Foundation for Nutritional Research; 1953.
- 37 Burgstahler AW, Freeman RF, Jacobs PN. Toxic effects of silicofluoridated water in chinchillas, caimans, alligators, and rats held in captivity. Fluoride 2008;40(1):83-8.
- 38 Krook LP, Justus C. Fluoride poisoning of horses from artificially fluoridated drinking water. Fluoride 2006;39(1):3-10. Cf. Burgstahler AW. Failure to diagnose fluoride poisoning in horses caused by water fluoridation [editorial]. Fluoride 2006;39(1):1-2.
- 39 Justus C, Krook LP. Allergy in horses from artificially fluoridated water. Fluoride 2006;39(2): 89-94.
- 40 Macicek P, Krook LP. Fluorosis in horses drinking artificially fluoridated water. Fluoride 2008;41(3):177-83.
- 41 Australian Government. National Health and Medical Research Council. A systematic review of the efficacy and safety of fluoridation. Part A: Review methodology and results, Part B: Excluded studies. Canberra: Australian Government. National Health and Medical Research Council; 2007.