Editorial

Chemosterilization: Spermatogenesis, Steroidogenesis, Reproductive Functions, and Behavior; from Historical Perspective to Contemporary Practice

The knowledge of the effect of chemosterilants on the testes and spermatogenesis is much less complete than on ovaries and oogenesis. The classical sterile male-techniques were based on the sterilization of male insects by irradiation, which were found to cause the rise of dominant lethal mutations that affect either entire chromosomes or individual chromatids. In those experiments, changes were not usually found on sperm, but most often they are evident in anomalies in the division of the zygote in the fertilized egg.[1] Dominant lethal mutations in *Cochliomyia hominivorax* (screw-worm) were described in detail in one of such classical experiments by LaChance and Riemann[1] and LaChance and Crystal.[2] Information and complications associated with dominant lethal mutations produced in insects by irradiations as well as sterilants were presented by LaChance, who has included a comprehensive bibliography comprising works that dealt with this topic long before the era of chemosterilants.[3]

Now-a-days, chemical castration is not at all considered as castration, because in it, no cutting is involved. It is generally considered reversible when treatment is discontinued. It has been found in various recent experiments that it reduces circulating levels of testosterone by chemical means. Androgens, testosterone, and dihydrotestosterone (DHT) are critical regulators of male sexuality. Both erection and ejaculation are influenced by testosterone levels.[4] Paradoxically, testosterone surge occurs with sexual activity.[5] Thus, steroid antiandrogen drugs, GnRH agonists reduce sex drive by blocking androgen receptors.

Thus, it is evident from the classical and recent experiments that chemosterilants affect testes and spermatogenesis. Because, the practical application of strong mutagens, as in classical experiments with insects, is out of the question; thus, the possibilities of using chemicals to produce azospermia or inactivation of sperm for male sterilization have been considered lately. The mechanism of these chemicals originate from papers published so far that spermatogonia and growing spermatocytes undergoing the division are mostly affected.[6,7] With the degeneration of spermatogenic cells, the entire testes become smaller.[8] In a classical experiment, Hamilton and Shutter reported the effect of apholate on accessory glands in *Diabrotica undecimpunctata* Howardii barbar (cucumber beetle). The accessory glands degenerate (as they are androgen dependent) and the transfer of sperm during copulation are blocked.[9] The recent experiments with animals also support the same.[6,10] Recent studies have also documented the oxidative stress inducing (i.e., reactive oxygen species generating) activities of some chemosterilants.[6,11] Some other studies reported the steroidogenesis inhibitory activities (basically 17β hydroxysteroid dehydrogenase and Δ^5-3β hydroxysteroid dehydrogenase inhibitory activities) of some chemicals.[6,8] Earlier experiments on the inductions of dominant lethal mutations also reported that the effects of chemosterilants on spermatogenesis are often followed by lowered vitality of sperm, which may lead to its immotility or even death.[2,3] In another experiment, Ascher *et al.* studied the degree of motility of sperm in spermatheca of *Musca domestica* (common housefly) females sterilized with Brestan and Tinicide. They found that the degree of fertility is in direct relation to the degree of motility of sperm.[10]

There are several chemosterilants that have used so far, but among the most useful chemicals are medroxyprogesterone acetate (MPA) and cyproterone acetate (CPA). MPA, also known by brand names Clinovir, Cycrin, Depo-Provera, and Hystron, is the hormone used for chemical castration in the United States. MPA was first introduced to the market for the treatment of some gynecological problems The Food and Drug Administration (FDA) withdrew MPA from the market in 1978. Outside the USA, MPA is available as birth control; although the FDA has never approved it for this use. Heller *et al.* first reported that progestational compounds decreased testicular size and suppressed male libido.[12] MPA reduces testosterone production by inhibiting gonadotropin secretion.[12] In addition, MPA accelerates testosterone metabolism in the liver leading to lower circulating levels of testosterone.[13] It was first administered as an intramuscular injection of about 400 mg weekly.[12,13] Effects are seen within 2–3 weeks of starting a course of MPA. In the historical study of Gagne using 48 participants, 40 participants positively responded to MPA and all participants experienced lowered sexual fantasy, arousal,

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and urges (particularly masturbation). MPA leads to a significant reduction in the number of ejaculations and circulating testosterone levels.[14] Alternatively, cyproterone acetate (CPA), marketed under the names Androcur, Cyprone, Cyprostat, and Dianette, is not officially approved in the United States, but is used in Canada, the United Kingdom, and Germany. Comparative studies of MPA and CPA are difficult because the drugs are not available in the same countries. In their seminal study on the clinical uses of CPA, Laschet and Laschet by using 100 mg oral doses daily or 300 mg intramuscularly every 2 weeks, observed significantly reduced or eliminated sexual desire, erections, and orgasms in 100 sexually deviant male participants. CPA decreases testosterone production by competitive inhibition of testosterone and DHT in androgen receptors. Like MPA, CPA suppresses sexual fantasies, libido, number of ejaculations, and spermatogenesis.[15]

Little is known about the behavioral effects of chemical castration. However, a few studies have been performed. In a recent study by Vinke *et al.*,[16] the effects of surgical and chemical castration on inter-male aggression, sexual behavior, and interaction behavior in the male ferret (European polecat) were assessed and compared. Chemical castration resulted in a reduction of inter-male aggression both in the presence as well as in the absence of a receptive female. Furthermore, chemical castration had a greater effect on the decrease of aggression than surgical castration.[16] In 2001, a study was performed to determine the effects of deslorelin treatment on the control of reproduction and sex-related behavior in exotic wild animals.[17] Although this study was remarkably short and small numbers of animals were involved, the following preliminary observations were made: antagonistic behavior in male sea otters ceased after treatment with a deslorelin implant, and no adverse effects were observed on social behavior in four male cheetahs treated with deslorelin.

Chemical castration in males is a reversible method of fertility regulation. Several drugs have been used and altogether they inhibit spermatogenesis and reduces libido. In most countries where the drugs have been used, they are used as punitive measures to reduce libido for sexual perverts like child molesters, rapist, and individual with hyper-sexuality.[18-21]

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REFERENCES

1. LaChance LE, Reimann JG. Cytogenetic investigations on radiation and chemically induced dominant lethal mutations in oocytes and sperm of the screw worm fly. Mutat Res 1964;1:318-33.
2. LaChance LE, Crystal MM. Induction of dominant lethal mutations in insect oocytes and spermby gamma rays and alkylating agent: Dose-response and joint action studies. Genet Res (Camb) 1965;51:699-708.
3. LaChance LE. The induction of dominant lethal mutations in insects by ionizing radiation and chemicals as related to sterile male technique in insect control. In: Wight, Pal, editors. Genetics of Insect Vectors of Diseases. Amsterdam; 1967; p. 617-50.
4. Rubinow DR, Schmidt PJ. Androgens, brain and behavior. Am J Psychiatry 1996;153:974-84.
5. Jannini EA, Screponi E, Carosa E, Pepe M, Lo Giudice F, Trimarchi F, *et al*. Lack of sexual activity from erectile dysfunction is associated with a reversible reduction in serum testosterone. Int J Androl 1999;22:385-92.
6. Sengupta P. Environmental and occupational exposure of metals and their role in male reproductive functions. Drug Chem Toxicol 2013;36:353-68.
7. Dutta S, Joshi KR, Sengupta P, Bhattacharya K. Unilateral and bilateral cryptorchidism and its effect on the testicular morphology, histology, accessory sex organs and sperm count in Laboratory Mice. J Hum Reprod Sci [In press].
8. Chandra AK, Sengupta P, Goswami H, Sarkar M. Effects of dietary magnesium on testicular histology, steroidogenesis, spermatogenesis and oxidative stress markers in adult rats. Indian J Exp Biol 2013;51:37-47.
9. Hamilton EW, Sutter GR. Chemosterilizing southern corn rootworm beetles with apholate. J Econ Entomol 1969;62:1285-8.
10. Ascher KR, Meisner I, Nissim S. The effects of fentins on the fertility of the male housefly. World Rev Pest Control 1968;7:84-96.
11. Chandra AK, Sengupta P, Goswami H, Sarkar M. Excessive dietary calcium in the disruption of structural and functional status of adult male reproductive system in rat with possible mechanism. Mol Cell Biochem 2012;364:181-91.
12. Heller CG, Laidlaw MW, Harvey HT, Nelson DL. The effects for progestational compounds of the reproductive processes of the human male. Ann N Y Acad Sci 1958;71:649-55.
13. Gijs I, Gooren L. Hormonal and psychopharmacological interventions in the treatment of paraphilias: An update. J Sex Res 1996;33:273-90.
14. Gagne P. Treatment of sex offenders with medroxyprogesterone acetate. Am J Psychiatry 1981;138:644-6.
15. Laschet U, Laschet L. Psychopharmacotherapy of sex offenders with cyproterone acetate. Pharmakopsychiatr Neuropsychopharmakol 1971;4:99-104.
16. Vinke CM, Deijk R, BB Houx Houx, Schoemaker NJ. The effects of surgical and chemical castration on intermale aggression, sexual behaviour and play behaviour in the male ferret. Appl Anim Behav Sci 2008;115:104-21.
17. Bertschinger HJ, Asa CS, Calle PP, Long JA, Bauman K, DeMatteo K, *et al*. Control of reproduction and sex related behaviour in exotic wild carnivores with the GnRH analogue deslorelin: Preliminary observations. J Reprod Fertil 2001;57:275-83.
18. "Court issues 1st chemical castration sentence". Korea Herald, 3 Jan 2013. Available from: http://nwww.koreaherald.com/view.php?ud=20130103000795 [Last accssed on 2013 May 13].
19. Sengupta P. Health Impacts of Yoga and Pranayama: An Art-of-the-state Review. Int J Prev Med 2012;3:444-58.
20. Chandra AK, Goswami H, Sengupta P. Dietary calcium induced cytological and biochemical changes in thyroid. Env Toxicol Pharmacol 2012;34:454-65.
21. "Russia introduces chemical castration for pedophiles". RT, 4 Oct 2011. Available from: http://rt.com/news/pedophilia-russia-chemical-castration-059/ [Last assessed on 2013 May 13].

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