
Workshops

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Pharmacological aspects of male contraception**Grootegoed *, J.A.***Department of Biochemistry II, Medical Faculty, Erasmus University Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands*

An acceptable anti fertility drug for men would have to be capable of reversibly suppressing sperm production and/or sperm function. Male fertility can probably be impaired most effectively through drug action on sperm maturation in the epididymis (rapidity of onset, reversibility), rather than on spermatogenesis in the testis. Several xenobiotic compounds that might act preferentially on epididymal sperm have been identified and tested. A notable example is α -chlorohydrin that has a rapid and reversible antifertility effect on male animals from several species, but also shows toxicity. At present, WHO collaborative research with Chinese investigators is carried out to characterize the active compounds from *Tripterygium wilfordii*, a herbal plant that has found widespread use in Chinese traditional medicine and that affects the fertility of human males without apparent inhibition of spermatogenesis.

Hormonal manipulation of epididymal sperm maturation is not feasible. The major regulator of epididymal function, plasma testosterone, is also required to maintain libido and other features of the health status of men. However, with respect to spermatogenesis the situation is very different. Interference with the production of testosterone by the Leydig cells strongly impairs spermatogenesis in a quantitative manner, also when plasma testosterone levels are maintained within the normal range through administration of a synthetic testosterone derivative.

The gonadotrophins LH and FSH are needed for maintaining the normal functioning of the testis, LH being the major regulator of Leydig cell steroidogenesis. Therefore, drugs which suppress the secretion of the pituitary gonadotrophins, given in combination with a synthetic testosterone derivative, will induce male infertility. In monkey studies, promising results have been obtained using a strong GnRH antagonist in combination with the WHO testosterone ester 20 AET-1 that has slow-release characteristics. Long term suppression of spermatogenesis in monkeys using hormonal methods has been found to be fully reversible. In clinical trials supported by the WHO Special Programme, sperm production in male volunteers is being suppressed for several months through injections with depotmedroxy progesterone acetate (DMPA) in combination with testosterone enanthate or other testosterone preparations. An early finding is that full suppression of sperm production (azoospermia) is obtained in more than 90% of the treated non-caucasian men, whereas only approximately 60% of the treated caucasian men show a complete absence of sperm. This possible ethnic difference of the response needs further study, as well as the requirement for azoospermia. It cannot be excluded that the residual sperm produced by men whose sperm production is only partially suppressed (oligozoospermia) are incapable of fertilizing ova.

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