BOOK REVIEWS

THERAPEUTIC SEX REDUCTION

By: K. FREUND, M.D., D. Sc.

In: Acta Psychiat. Scand. 287, Vol. 62

Sex drive reducing therapies are employed in those cases of anomalous erotic preferences in which the patient's sexual behaviour is dangerous or while not really dangerous, is utterly unacceptable to the community or is an embarrassment to the patient himself. There are three basic approaches to radical sex drive reduction.

I. Pharmacological Sex Drive Reduction:

Foote (1944) used oestrogen, however this invariably led to gynecomastia. Heller **et al.** (1958) employed progesterone derivatives, while Laschet & Laschet (1967) introduced cyproterone acetate (Androcur), and servais & Hubin (1965, 1968) used methylestrenolone.

Cyproterone acetate 100 mg daily produced very considerable reduction of sex drive in 80%, while 20% of cases needed 200 mg daily for a comparable effect (Laschet & Laschet 1969) which starts after a week. 300-500 mg of oily solution given I.M. at 7-14 days interval is therapeutically equivalent to 100-200 mg orally per day (Laschet & Laschet 1975). These workers, in a report on cyproterone acetate treatment of 300 men, some followed up to 8 years, indicate that the drug is well tolerated by the liver but, during the 2nd to 6th week of treatment, there is sometimes increased fatiguability, an increased requirement of sleep, increased appetite, and sometimes a slight depression, and in 20% of the cases some gynecomastia.

Cyproterone as well as cyproterone acetate are antiandrogens, i.e.

compounds which prevent the action of androgens at target organ level. This effect would appear to be limited to the genital and accessory genital organs.

Medroxyprogesterone acetate, (Depot Provera) 300-400 mg I.M. every 10 days, is not an antiandrogen. Both compounds reduce sex drive by reducing the level of circulating testosterone. 100 mg of cyproterone acetate per day orally lower the level of circulating testosterone to about one-fifth of the normal. It is well known that in human males a gross decrease in plasma testosterone level leads to a gross decrease in sexual behaviour and that in these cases a substantial increase in testosterone supply leads to sexual activation (Davidson et al. 1979).

Low (though not extremely low) plasma testosterone levels need not necessarily be accompanied by lower levels of sexual activity. Raboch and Starka (1972) found no significant difference, on frequency of intercourse, between normal controls and patients having varicocele and therefore, very low testosterone levels, and they drew the conclusion that in the physically mature male testosterone is present in much greater amounts than is needed for normal frequency of intercourse.

Investigations of the more intricate aspects of the relationships between concurrent testosterone level and sexual stimulation and behaviour render more conflicting results than clear information. Change of plasma testosterone level as a consequence of sexual stimulation was demonstrated by Kraemer et al. (1976), these investigators concluded that, for every individual, there might exist a critical testosterone level below which a subject starts to generate activity, which in turn elevates plasma testosterone level. In contrast, automasturbation had no significant effect on testosterone level. These findings would appear to indicate that the crucial testosterone increasing stimulus is not penile friction or orgasm, but the preceding stimulation. Pirke et al. (1974) measured plasma testosterone level before, during and after presentation of a sexually stimulating movie and found an average increase of 36% of the subjects' pre-experimental testosterone level and no increase of testosterone level in controls who viewed a sexually neutral film.

LaFerla (1977) found increased level of luteinizing hormone and Follicle stimulating hormone in males to whom an arousing sex film was shown. In contrast, Lincoln (1974) did not find such increase in L.H. or testosterone in a similar situation.

Cyproterone acetate reduces substantially the output of F.S.H. (Rausch-Stroomann et al. 1970) which in turn leads to a substantial reduction in sperm count. Medroxyprogesterone acetate inhibits both L.H. output and F.S.H. output. Both compounds reduce production of testosterone from its precursors.

Although the testosterone reducing effect of cyproterone acetate and medroxyprogesterone acetate makes it likely that their application leads to sex drive reduction, the extent of this behavioural impact is still uncertain. It would appear that research in this realm should follow mainly two lines, one towards developing drugs, which would decrease circulating testosterone more efficiently, and a second line which is to develop antiandrogenic drugs which would interfere mainly with the impact of the patient's own testosterone on those brain structures which are most directly involved in mediating sexual approach behaviour.

fl. Removal of The Gonads :

Castration is of a high degree of efficiency and permanence in keeping sex drive at a minimum. In contrast, the majority of patients on pharmacological sex drive reducers drop out from this treatment within one or two years. Oddly enough, however, the question to what extent, if any, gonadectomy reduces male sexual approach behaviour has not yet been answered unequivocally by pertinent animal experiments. Relatively recent topic related animal experimentation addresses itself to fading out of various behavioural components, and not directly to reduction of sexual approach behaviour in general.

Fading out of sexual behaviour in castrated animals :

There is still not very much information as to how long appreciably

intense sexual appetite can outlast removal of the gonads, and how exactly the behavioural pattern will change over time. Coyotupa et al. (1973) reported that testosterone and dihydrotestosterone plasma levels in rats decreased about 50% within 5 minutes after gonadectomy.

Beech (1970) supplied a brief comprehensive overview of what is known about patterns, and rates of change, of mating behaviour in castrated male mammals. Penile intromission seems to be possible somewhat longer than ejaculation. Although this difference is small in rats, it is appreciable in guinea pigs, and particularly in rabbits. According to Beech, male rodents, cats and dogs continue to mount long after intromission has disappeared. Beech himself observed castrated (male) dogs for 21 to 36 months. Within six months there was an appreciable decrease in intromission frequency and the length of time erection was maintained. However, "these behavioural measures showed no further decline in two and a half years".

Phoenix et al. (1973) found a substantial overall decline in regard to virtually all aspects of sexual behaviour in all 10 cases of castrated male rhesus monkeys. However, the individual animals were very differently affected, with two animals no ejaculations could be elicited after castration, while on the other extreme there were two animals who were able to ejaculate one year after castration. This interindividual variability of the effect of castration exists in other species as well.

As to the possibility of reawakening sex drive by testosterone treatment, experiments by Hutchinson (1974a, b) on castrated doves, support the notion of decreasing behavioural responsiveness to testosterone. According to Neumann & Steinbeck (1971), this also holds for mammals.

Fading out of sexual behaviour in humans :

Sturup (1972) found that castration is very successful in mentally defective sex offenders, but is not successful in schizophrenic sex offenders, and that contrary to what is true for other criminal offenders, recidivism does not diminish with age.

Recidivism rate was found to range from 1.1-2.2% in a 900 case study by Sand **et al.** (1964). Bremer (1959) found that recidivism rate before castration was 58% and after castration about 3%, a large proportion of Bremer's 215 cases were mental defectives.

The degree to which sex drive level decreases depends on the length of time of testosterone deprivation, and it would appear to be possible to further decrease recidivism rate be detaining patients for appropriate periods of time after surgery.

Hackfield (1933) was probably the first to point out that the sex drive reducing effect of castration usually does not show immediately after surgery, but develops slowly over a period of time.

Apart from pointing out the necessity of taking into account the interval between gonadectomy and its behavioural impact, Hackfield was probably also the first to specify that even if castration does not lead to virtually full eminiation of sexual behaviour or sexual urges, this intervention fulfills its task if it decreases sex drive sufficiently to enable the patient to refrain from acting-out his anomalous, socially unacceptable (or dangerous) erotic urges. Therefore, the fact that intercourse sometimes may be possible for many years after castration does not necessarily mean that insufficient sex drive reduction was brought about by the intervention.

Short term and long term side effects :

The most frequent complaints were about slight permanent depression or depression lasting only for a short time after surgery, hot flushes for several months after surgery, and about permanent difficulties in concentration. Langeluddeke (1963) found that nearly 10% developed a more female type of fat distribution and/or considerable gynecomasty. About one-quarter of his cases developed the typical excessively wrinkled "castrate face". In about 50% the distribution of pubic hair changed from male to female type. In a large number osteoporosis was diagnosed. However, the cosmetic effect of an empty scrotum and even the ensuing erectile impotence can nowadays be taken care of by plastic surgical methods.

III. Surgical Intervention at Central Regions of The Mating System :

Some of the information gathered on the central parts of the reproductive system appreared therapeutically promising in that circumscribed lesions in particular areas of the brain radically decrease sex drive level, without any appreciable decrease of circulating testosterone. These structures are located in the hypothalamus.

The medial area preoptica has been shown to be of crucial importance for male sexual behaviour in fish, amphibia, birds and mammals (Kelly & Pfaff 1978). The anterior hypothalamus and the ventromedial nucleus of the hypothalamus are of greater importance for the lordosis response, the most frequently occurring part of ahe typically female copulatory pattern. According to Whalen (1976) the lordosis response could be elicited in (spayed) female rats, guinea pigs, cats and rabbits by estradiol implants from as far frontally as the bed nucleus of the diagonal band to the more caudally situated premammillary region and the mammillary, bodies. These implants were mostly effective in this respect in the ventromedial nucleus of hypothalamus (Sawyer 1963; Barfield & Chen 1977). In female rabbits and rhesus monkeys, not only estradiol but also testosterone implants in ventromedial nucleus facilitates the lordosis response (Palka & Sawyer 1966). Testosterone implants in medial-preoptic-anterior-hypothalamic region can almost fully reactivate mating behaviour in castrated male mammals (Davidson 1966; Kierniesky & Gerall 1973). Similar implants at other sites of the brain result in only marginal revival of male mating behaviour or no such revival at all. It is therefore safe to conclude that these hypothalamic sites are particularly rich in specific sex hormone receptors (Pfaff 1967; Pfaff & Keiner 1973).

Electrical stimulation of the area preoptica elicits, in the male animal, mounting and copulatory behaviour (Fisher 1956; Malsbury 1971). It also results in an upsurge of the luteinizing hormone level in rats of both sexes, and in ovulation in the female.

Electrical coagulation of the area preoptica resulted in cessation of

sexual activity without testicular atrophy, i.e. without gross hormonal changes, in male rats (M.L. & H. Soulaire 1963). This findings was confirmed by Larsson & Heimer (1964) for large lesions involving the medial-anterior hypothalamic continuum. Small lesions resulted only in temporary cessation, or impairment, of mating behaviour, and according to Larsson & Heimer (1964), coagulation in the lateral area preoptica did not diminish sexual behaviour in 9 of 11 male rats.

Electrical coagulation in the anterior hypothalamus abolished mating behaviour in female rabbits and cats. Coagulation of the posterior part of hypothalamus involving the ventromedial nucleus abolished penile intromission and ejaculation without causing hormonal changes in male guinea pigs (Phoenix 1961). Cessation of sexual behaviour without ovarial atrophy occurred in female rabbits also, after coagulation in the posterior hypothalamus in particular the mammillary bodies (Sawyer & Robinson 1956).

Thus, one would expect that male mating behaviour can be most efficiently abolished without gross consequences for the hormonal system by destruction of tissue in the area preoptica, and it would appear that lesion of any other hypothalamic site would be far less reliable in appreciably reducing sex drive in males, without greatly interfering with the metabolism of sex hormones.

Roeder (1966) was the first to report on stereotaxic brain surgery in a homosexually pedophilic patient who indicated, after one sided coagulation of the ventromedial nucleus, that his erotic fantasy life was abolished and he had lost his homosexual pedophilic urges. The only side effect was that "potency was weakened (but preserved)".

Orthner reported in 1979 on results of the indicated surgical intervention in 34 patients. sex drive reduction was achieved in almost all cases.

Side Effects: No persistent interference with pituitary function was observed. There was persistent increased appetite leading to obesity. Tem-

porary diabetes insipidus caused by the postoperative local edema. Soon after surgery some patients became quite hostile. A number of patients indicated that since the operation they do not dream any more. No gross impairment of erectile capability was encountered. The operation did cause, almost always, an appreciable delay of the ejaculatory reflex, and orgasm ceased to occur in spite of strong erection.

REFERENCES

Barfield, R.J. & J.J. Chen (1977) Activation of estrous behaviour in ovarectomized rats intracerebral implants of estrodiol benzoate. *Endocr nology* 101, 1716-1725.

Beach, F.A. (1970) Coital behaviour in dogs: VI. Long-term effects of castration upon mating in the male. *J. Comp, Physiol. Psychol Monograph.* 70, Part 2 (32 pp.).

Bremer, J. (1959) Asexualization : A follow — up study of 244 cases. *Macmillan Company. New York.*

Coyotupa, J., A.F. Parlow & N. Kovacic (1973) Serum testosterone and dihydrotesterone levels following orchiectomy in the adult rat. *Endocrinology* 92, 1579-81.

Davidson, J.M. (1966) Activation of male rat's sexual behaviour by intracerebral implantation of androgen *Endocrinology* 79, 783-794.

Davidson, J.M., C.M. Camargo & E.R. Smith (1979) Effects of androgen on sexual behaviour in hypogonadal men. *J. Clin. Endocrinol. Metap.* 48, 955-958.

Fisher, A.E. (1956) Maternal and sexual behaviour induced by intracranial chemical stimulation. *Science* 124, 228-229.

Foote, R.M. (1944) Diethylstilbestrol in the management of psychopathological states in males. *J. Nerv. Ment. Dis* 99, 928-935.

Hackfield, A.W. (1933) Uber die Kastration bei Vierzig Sexuell Abnormen. Monastsschr, *Psyhiatr. Neurol.* 87, 1-31.

Heller, C.G., W. M. Laidlaw, H.T. Harvey & W.O. Nelson (1958) Ef-

fects of progestational compounds on the reproductive processes of the human male. *Ann. Acad. Sci.* 71, 649-665.

Hutchinson, J.B. (1974a) Post-castration decline in behavioural responsiveness to intrahypothalamic androgen in doves. *Brain Res.* 160-181.

Hutchinson, J.B. (1974b) Effect of photoperiod on the decline in behavioural responsiveness to intra-hypothalamic androgen in doves (streptopelia risoria). *J. Endocrinol.* 63, 583-584.

Kelly, D.D., & D.W. Pfaff (1978) Generalization from comparative studies on neuroanatomical and endocrine mechanisms of sexual behaviour. In Hutchinson, J.B. (ed.) (1978) : Biological determinants of sexual behaviour. John Wiley & Sons, Toronto.

Kiernicsky, N.C., & A.A. Gerall (1973) Effects of testosterone proprinate in the brain on the sexual behaviour and peripheral tissue of the male rat. *Physiol. Behav.* 11, 633-640.

Kraemer, H.C., H.B. Becker, H. Brodie, H. Keith, C.H. Doering, R.H. Moos & D.A. Hamburg (1976) Orgasmic frequency and plasma testosterone levels in normal males. *Arch. Sex. Behav.* 5. 125-132.

LaFerla, J.J., D.L. Anderson & D.S. Schalch (1978) Psychoendocrine response to sexual arousal in human males. *Psychosom Md.*, 166-172.

Lengeluddeke, A. (1963) Die Entmannung von Sittlichkeitsverbrechern in Deutschland. In Die Entmannung von Sittlichkeitverbrechern. De Gruyter, Berlin.

Larsson, K., & L. Heimer (1964) Mating behaviour of male rats after lesions in the preoptic area. *Nanr.* 202, 413-414.

Laschet, U., & L. Laschet (1967) Antiandrogentherapie der Pathologisch Gesteingerten und Abartigen Sexualitat des Mannes. Kurze wissenschaftliche Mitteilungen Klin. *Wochenschr* 45, 324-325.

Laschet, U., L. Laschet (1969) Three years clinical results with cyproterone acetate in the inhibiting regulation of male sexuality. *Acta Endocrinol. Suppl.* 138, p. 103.

Laschet, U., & L. Laschet (1975) Antiandrogens in the treatment of sexual deviations in men. *Steroid Biochem* 6, 821-826.

Lincoln, G.A. (1974) Luteinizing hormone and testosterone in man. *Nature*, 252, 232-233.

Malsbury, C.W. (1971) Facilitation of male rat copulatory behaviour by electrical stimulation of the medial preoptic area. Physiol. Behav. 7, 797-805.

Neumann, F., & H. Steinbeck (1971) Antiadrogene. Tierexperimentelle Grundlagen und klinische Anwendungsmoeglichkeiten. *Der Internist*. 12, 198-205.

Orthner, H. (1979) Sexual disorders. In Walker, H. (ed.) (In Press 1979): Textbook of stereotaxy of the human brain. University of New Mexico, Albuquerque.

Palka, Y.S., & C.H. Sawyer (1966) The effects of hypothalamic implants of ovarian steroids on oestrous behaviour in rabbits. *J. Physiol (London)* 185, 252-269.

Pfaff, D.W. (1976) The neuroanatomy of sex hormone receptors in the vertebrate brain. In Kuman, A. (ed.) 1976) :*Neuroendocrine Regulation of Fertility. Karger, Basle*, pp. 30-45.

Pfaff, D.W., & M. Keiner (1973) Atlas of estradiol-concentrating cells in the central nervous system of the female rat. *J. Comp. Neurol* 1951, 121-158.

Phoenix, C.H. (1961) Hypothalamic regulation of sexual behaviour in male guinea pigs. *J. Comp. Physiol. Psychol.* 54, 72-77.

Phoenix, C.H., A.K. Slob & R.W. Goy (1973) Effects of castration and replacement therapy on sexual behaviour of adult male rhesuses. *J. Comp. Physiol Psychol.* 84, 472-481.

Pirke, K.M., G. Kochott & F. Dittmar (1974) Psychosexual stimulation and plasma testosterone in man. *Arch. Sex. Behav.* 3. 577-584.

Raboch, J., & L. Starka (1972) Coital activity of men and the levels of plasmatic testosterone. *J. Sex. Res.* 8, 219-224.

Rausch-Stroomann, J. G., R. Petry, V. Hocevar, J. Mauss & T. Senge

(1970) Influence of an antiandrogen (cyproterone) on the gonadotrophic function of the pituitary gland, on the gonads and on metabolism in normal men. *Acta. Endocrinol.* 63, 595-508.

Roeder, F.D. (1966) Stereotaxic lesion of the tuber cinereum in sexual deviation. *Confin. Neurolog.* 27, 162-163.

Sand, K., Dickmeiss & P. Schwalbe-Hansen (1964) In Bataenkning om sterilisation ogkastration. *Publication* No. 353, 46-57, 1964. (According to Sturup, 1968).

Sawyer, C.H. (1963) Induction of estrus in the ovariectomized cat by local hypothalamic treatment with estrogen. *Anat. Rec.* 145, p. 208.

Sawyer, C.H., & B. Robison (1956) Separate hypothalamic areas controlling pituitary gonadotrophic function and mating behaviour in female cats and rabbits. *J. Clin. Endocrinol. Metab.* 16, 914-915.

Servais, J., & P. Hubin (1965) Etude psychopharmacologique de la methyestrenolone inhibiteur de la libido chez l'homme normal, *Acta Neurol. Belg.* 65, 983-995.

Servais, J., & P. Hubin (1968) Synthese des connaissances actuelles concernant un inhibiteur de la libido chez le male, la mythyloestrenolone. *Encephale* 57, 334-352.

Soulairac, M.L. (1963) Etudes experimenale des regulations hormononervouses du comportement sexual du rat male.*Aunal. Endocrino* 24, *Suppll.*, 1-98.

Sturup, G.K. (1972) Castration : The total treatment. In Resnik H.L.P., and M.E. Wolfgang (eds.) (1972) : Sexual behaviors : Social, clinical and legal aspects. Little, Brown & Co., Boston, pp. 361-382.

Whhalen, R.E. (1976) Brain mechanisms controlling sexual behaviour. In Beach, F.A. (ed.) (1976) : Human sexuality in four perspectives. *Johns Hopkins University Press. Baltimore.*

Summarized by : N.A. Youssef, M.B. D.P.M.
Senior Registrar, Kekma Hospital

(رقم ايداع المجلة الطبية المصرية ١٨٦ / ٧٧)

المطبعة الفنية الحديثة
٢٠ شارع الأمير في بالفجالة ت ٨٦٤٨٨١