INHIBITION OF SPERMATOGENESIS IN MEN WITH MONTHLY INJECTIONS OF MEDROXYPROGESTERONE ACETATE AND TESTOSTERONE ENANTHATE

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ABSTRACT

Twenty-five healthy men were treated with monthly injections of 100 mg of medroxyprogesterone acetate (MPA) and 250 mg of testosterone enanthate (TE) for periods from 4 to 16 months. In 24/25 subjects, a marked drop in sperm count occurred by 1-3 months following the first combined injections of MPA and TE. Eleven subjects out of 14 who completed 9 months of treatment became azoospermic or developed marked oligozoospermia. Of the 8 men treated for 12-16 months, only one failed to respond to the treatment. Two subjects reported decreased libido and potency; 4 subjects reported increased libido and potency. There were no changes in the size, consistency or sensitivity of the testicles or breasts. No significant changes occurred in serum transaminases or in alkaline phosphatase during the treatment. With 2 possible exceptions, serum triglycerides also seemed to be unaffected by treatment. There were no changes in blood pressure. Weight gain was common.

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INTRODUCTION

Medroxyprogesterone acetate (MPA) is a potent progestin which has been widely used as a long-acting contraceptive in women (1,2). The drug reduces gonadotropin secretion, thereby suppressing the midcycle LH peak and inhibiting ovulation in women for 6 months or longer following a single injection of 400 mg MPA (3). The agent was also found to reduce sperm levels in men in limited clinical trials (4). In the present study, we tested the antispermatogenic effect of MPA in a group of fertile men who volunteered for the clinical trial. Injections of testosterone enanthate (TE) were given concomitantly, in order to offset any effects of diminished endogenous testosterone resulting from MPA-induced inhibition of gonadotropin release. It was also hoped that TE would enhance the inhibition of gonadotropin release, thereby increasing the antispermatogenic effect (4).

METHODS

Twenty-five healthy volunteers, 21 to 41 years of age (average 31), were accepted for this study. Each subject had fathered at least 2 children. The subjects received 100 mg medroxyprogesterone acetate (150 mg/ml, Depo Provera, Upjohn) and 250 mg testosterone enanthate (Delatestryl, Squibb) in separate intramuscular injections at monthly intervals. Sperm counts and motility were determined prior to initiation of treatment and before each pair of monthly injections. Breasts and external genitals were examined at each visit. Subjects were questioned about coital frequency, and changes in sexual desire and potency. Body weight and blood pressure were determined. Serum levels of alkaline phosphatase, transaminases (SGOT and SGPT), and triglycerides were determined at regular intervals during the treatment.

RESULTS

In 24/25 subjects, a marked drop in sperm count and in sperm motility occurred by 1-3 months following the first combined injections of MPA and TE. At the end of 4 months of treatment, 6/19 men (31%) had reached azoospermia or severe oligozoospermia (1 million sperm/ml or less). By the sixth month of treatment, this number had increased to 11/18 (61%). After 9 months of treatment, 11/14 subjects (79%) had become azoospermic or developed marked oligozoospermia. Of the 8 men treated for 12-16 months, all but one subject responded to the treatment. Figures 1-3 depict the typical pattern of initial decrease in sperm count, the variations in the time required to achieve a marked decrease, and the tendency to maintain this low level with continued treatment. The sperm counts for the unresponsive subject are shown in Fig.4. He not only maintained a high sperm count throughout the treatment, but developed no changes in sperm motility which would indicate an alteration in the fertilizing capacity of the spermatozoa. This subject had no clinical signs of endocrinopathy, and liver function tests remained at normal levels throughout treatment.

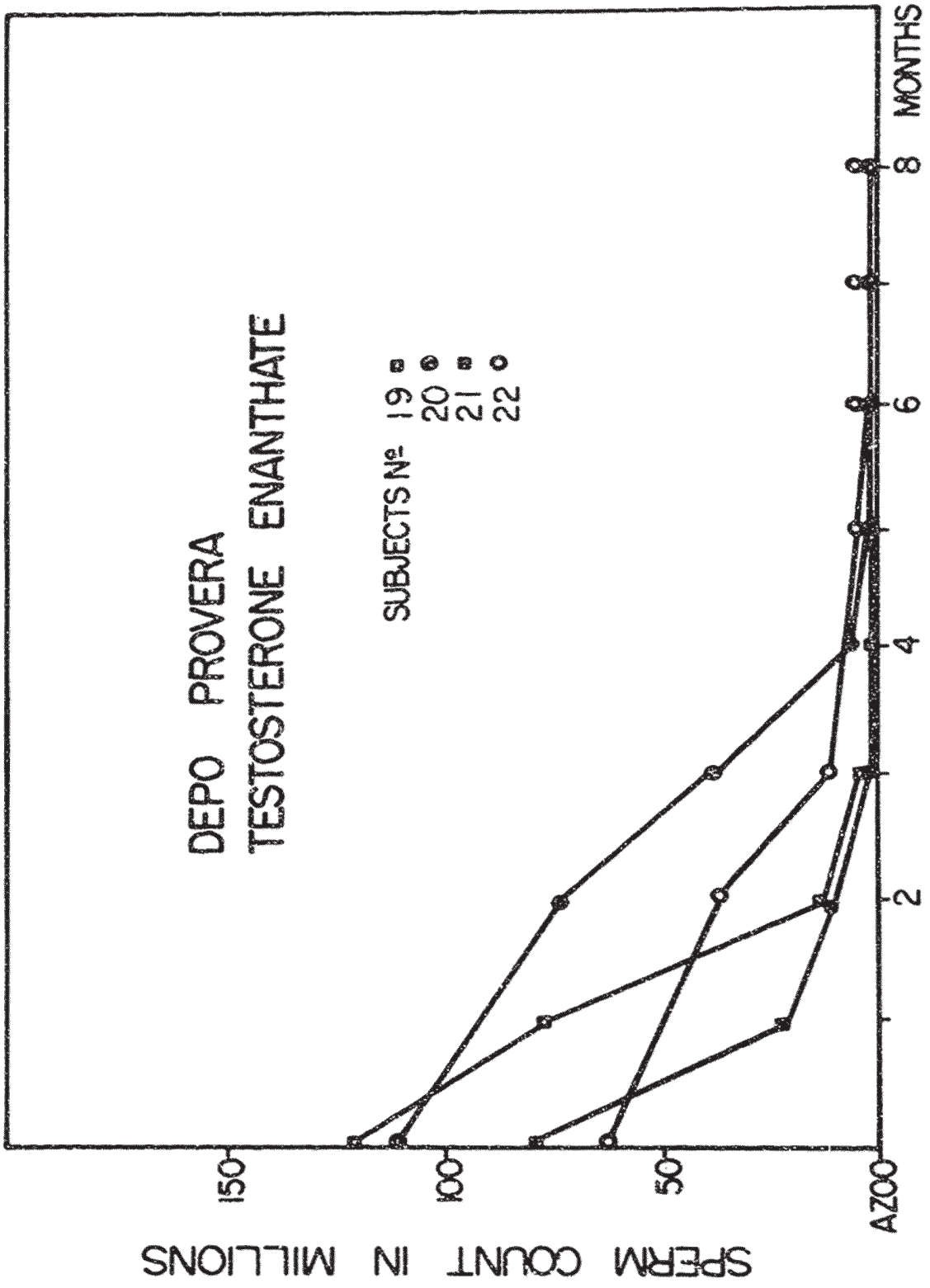

Fig.1 - Sperm counts in men receiving monthly MPA and TE injections. Note that subject 20 took almost two months longer than subjects 19 and 21 to reach azoospermia.

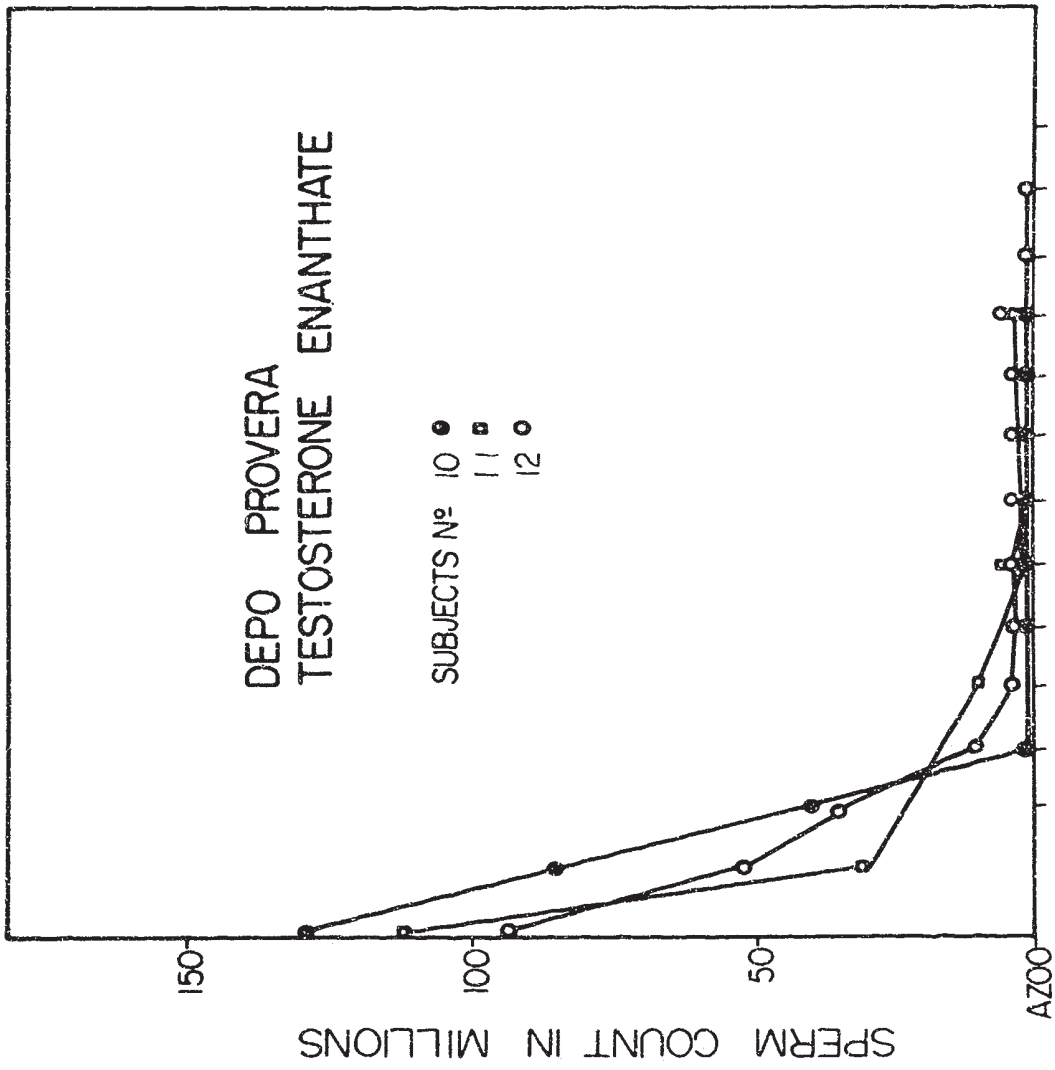

Fig.2 - Typical drop in sperm counts in men receiving monthly MPA and TE injections.

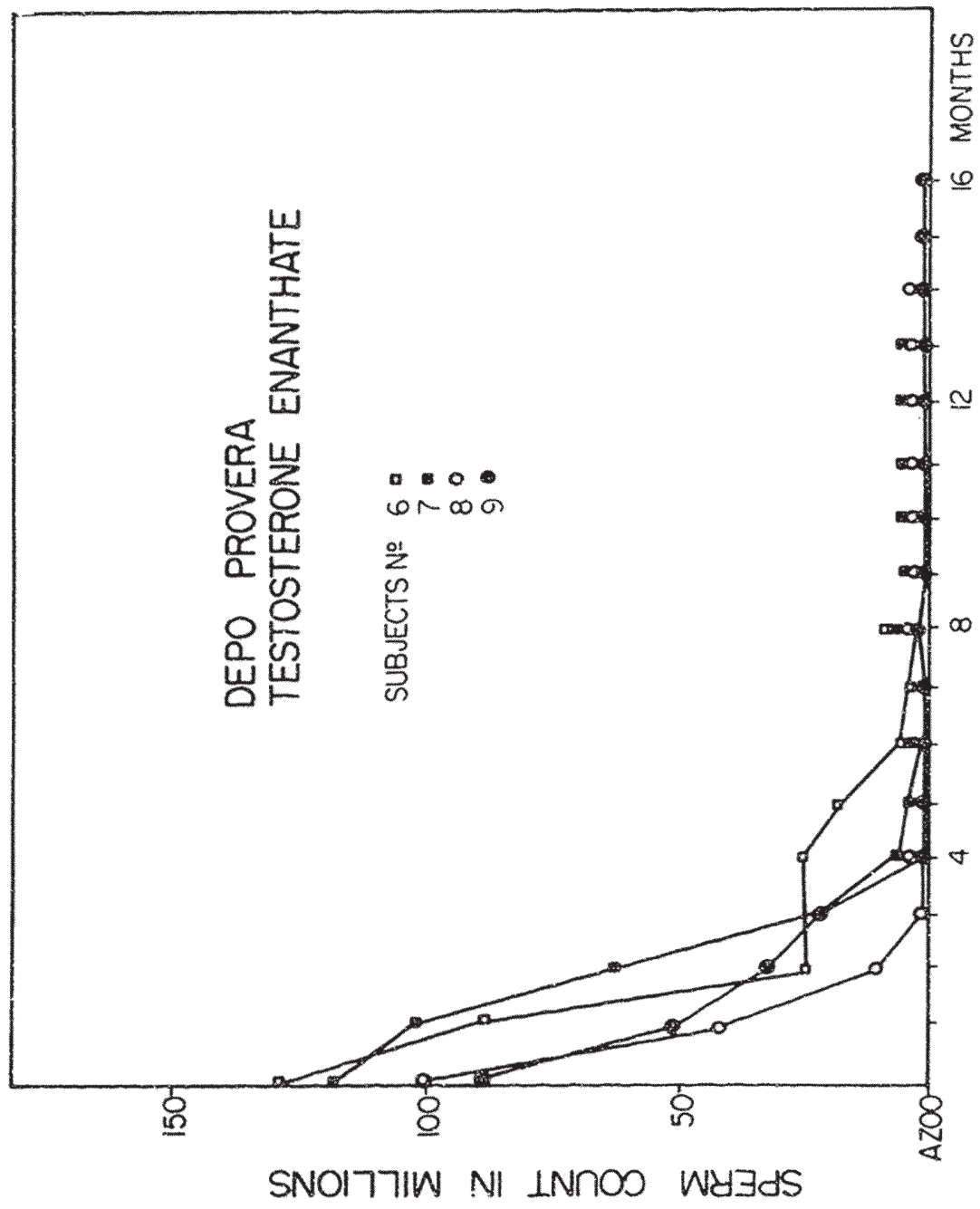

Fig.3 - Sperm counts in men receiving monthly MPA and TE injections. Note that subjects 7, 8 and 9 were azoospermic for six months or longer.

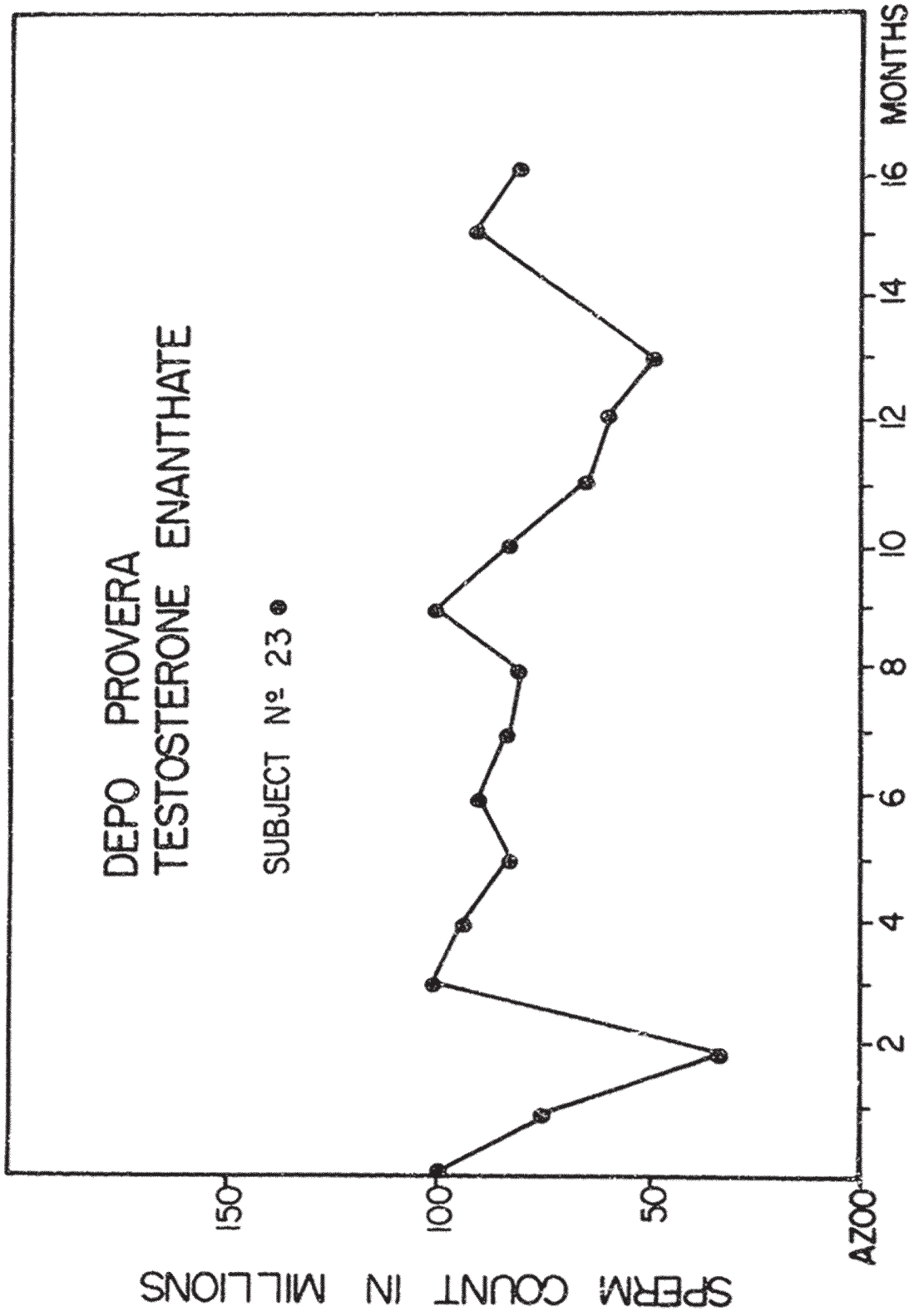

Fig.4 - Sperm count of a subject receiving monthly MPA and TE injections. Note that sperm counts of this subject remained apparently unaffected by the monthly injections.

Two subjects reported decreased libido and potency, and decided to discontinue treatment for that reason. Four other men reported a transient decrease in libido and potency, but had recovered by the next visit, 30 days later. Five subjects reported increased libido. Four of these 5 also reported increased potency. There were no changes in the size, consistency or sensitivity of the testicles or the breasts.

Moderate weight gain occurred in most patients. The mean weight increase was 2 kg in one year. The maximum weight increase was 5 kg for one patient in one year. There were no changes in blood pressure in any subject.

No significant changes occurred in SGOT, SGPT, or alkaline phosphatase levels during the treatment. In all but 2 subjects, no significant changes occurred in serum triglycerides during treatment. In one subject, the level of triglycerides rose from 56 to 147 mg% and remained at this higher level throughout the treatment period. In another subject, triglycerides rose from a pre-treatment level of 46 to 134 mg%, and later dropped to 101 mg% during treatment. However, these higher levels remained within normal limits.

Information is available on return to fertility in one subject. His sperm count dropped from 80 million/ml virtually to zero by the fourth month; contact with the subject was lost at the sixth month. Three months following the last injections, his wife became pregnant, and subsequently gave birth to an apparently normal son. Several months after the birth (more than one year following discontinuation of treatment), the subject provided a semen specimen in which the sperm count was 105 million/ml. Motility was 80%, compared with the pre-treatment value of 60%.

DISCUSSION

Previous studies have shown that it is possible to induce azoospermia in men by inhibiting gonadotropin secretion without a corresponding suppression of libido and potency (5,6,7). Our own trials with combination treatments of testosterone implants and various 19-nor-steroids indicated that azoospermia or severe oligozoospermia could be induced and maintained for several months in young men (7). Spermatogenesis was restored within a few weeks following discontinuation of treatment.

A major problem with the various 19-nor-steroid regimens has been the need for frequent (weekly) administration of high doses, which may represent an extreme challenge to the liver. The present injection treatment gives slow release of the hormones, and reduces the total amount of steroid to which the liver is exposed at any particular time. Medroxyprogesterone acetate doses of 150 mg/3 months and 400 mg/6 months are considered non-toxic in women for long-term contraceptive use (1,2,3). The doses of medroxyprogestrone acetate and testosterone enanthate used in the present clinical trials have been well-tolerated in men treated for as long as one year.

Major problems to be resolved are those associated with incomplete suppression of spermatogenesis in some subjects, and the need for repeated sperm counts as the only way to evaluate the effectiveness of the treatment. Although discontinuation of treatment is followed by an increase in sperm count, and there is one known instance of a wife's pregnancy, the question of full reversibility in all subjects after long term spermatogenic suppression remains to be established.

ACKNOWLEDGEMENT

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