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Depot-Leuprolide Acetate for Treatment of Paraphilias: A Report of Twelve Cases

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A new class of antiandrogen medications, gonadotropin-releasing hormone agonists, offers promise in the treatment of the paraphilias, with substantially less side effects than medroxyprogesterone acetate or cyproterone acetate. This paper reports the results of treatment using a depot suspension of leuprolide acetate on 12 patients with paraphilic disorders or with sexual disorders not otherwise specified to suppress or help these individuals control their deviant sexual behavior or impulses. The method involved uncontrolled observations of individuals treated with depot-leuprolide acetate for various lengths of time, from 6 months to 5 years, with the follow-up intervals ranging from 6 months to 6 years. Leuprolide acetate resulted in a significant suppression of deviant sexual interests and behavior as measured by self-report and was well tolerated. However, the three patients who were on long-term therapy developed bone demineralization, suggesting that this is a significant side effect of prolonged therapy. Leuprolide acetate shows promise as a treatment for the paraphilias.

KEY WORDS: sex offenders; paraphilia; leuprolide acetate; antiandrogens; LHRH agonists.

INTRODUCTION

The paraphilias are a significant source of social costs (Bradford, 1998) and victimization (Rosler and Witztum, 1998), as well as personal distress for individuals with these disorders. Surgical castration and antiandrogen agents have been used to treat these disorders (Bradford, 1985, 1988), but have substantial adverse side effects (Gijs and Gooren, 1996). Recently, a number of reports have detailed the use of gonadotropin-releasing hormone agonists to treat the paraphilias. Although several

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of these agents have been synthesized and are available, their actions are similar (Ascoli and Segaloff, 1996). Three groups have reported on the use of triptorelin (Rosler and Witztum, 1998; Thibaut *et al.*, 1993, 1996). Rousseau *et al.* (1990) reported on the use of LHRH ethylamide. Single case-reports of use of leuprolide acetate for the treatment of a patient with exhibitionism and Huntington's Disease (Rich and Ovsiew, 1994), and of patients with pedophilia (Cooper and Cernovsky, 1994, Dickey, 1992) have been described. We present herein the use of leuprolide acetate to treat 12 individuals with paraphilic disorders or with sexual disorders not otherwise specified.

METHODS

Patients were obtained through consultation with a state hospital system or from a private practice with a specialty of treatment of individuals with paraphilias. The decision to administer depot-leuprolide acetate was made on a case-by-case basis after appropriate treatment options were presented to individual patients or to those designated to consent for them. Informed consent was obtained for all patients treated. All individuals consented to the depot-leuprolide acetate without any court or legal mandate for this specific treatment, and all individuals had clinically identified problems of a paraphilia or of a sexual disorder not otherwise specified.

Baseline physical and laboratory examinations that included testosterone, follicle-stimulating hormone, and lutenizing hormone levels, and blood chemistries were obtained prior to inception of leuprolide acetate treatment except as indicated, and at variable intervals thereafter. Standard radioimmune assay techniques were used by the commercial laboratories performing the laboratory evaluations. Patients were referred to their attending medical physicians for an evaluation to assess and address the risks of leuprolide acetate treatment. Beginning in 1999, baseline bone density evaluations were additionally obtained as part of a baseline examination to assess for the development of osteopenia and osteoporosis, both side effects of prolonged antiandrogen therapy. Three patients treated for 3, 4, and 4.5 years had a bone density evaluation to assess for osteoporosis; only one of these had a baseline bone density evaluation prior to the inception of therapy.

To counteract a surge of follicle-stimulating hormone and lutenizing hormone, and thus testosterone, each patient was treated with flutamide, 250 mg by mouth three times per day for 30 days, beginning on the day of inception of depot-leuprolide acetate treatment. The flutamide was then discontinued. Leuprolide acetate was administered at a dose of 7.5 or 3.75 mg intramuscularly at monthly intervals.

All initial clinical assessments and ratings were based on direct clinical interviews; subsequent assessments were based on either direct interview or on

consultation with the patients attending psychiatrist or other caregivers. All diagnoses were made according to *DSM-IV* (American Psychiatric Association, 1994).

Some individuals received other treatments for their paraphilias, including weekly cognitive–behavioral group therapy or individual supportive therapy and monthly relapse-prevention therapy, and received treatment for other medical and mental disorders as was indicated.

RESULTS

All baseline medical examinations and laboratory assessments, which were obtained were reported as being within normal limits; in some instances baseline endocrine or laboratory measurements were not obtained or exact values were not recorded. Normal limits for reported laboratory measurements varied because different laboratories were used for various patients.

The cases are summarized in the accompanying table (Table I).

Patient #1 was a 40-year-old male with diagnoses of borderline personality disorder, alcohol dependence, and in the distant past cocaine and opiate dependence, recurrent major depression, and dysthymia, with eight psychiatric hospitalizations. He had had a history of pedophilia since his early teens, with a specific interest in pubescent males; he also had a self-reported homosexual orientation with a lesser interest in adult males. He reported recurrent sadistic sexual fantasies involving pubescent males, which had been present for more than 20 years. He had a history of phenytoin-induced liver failure and of hepatitis B and hepatitis C, with normal liver function tests. He had previously been on fluoxetine, 60 mg/day, for a 1-year period without effect on his deviant sexual fantasies; this had been discontinued a year prior to his presentation. He received depot-leuprolide acetate, 7.5 mg, for a 10-month period. He was also assessed as being depressed and was treated concomitantly with fluoxetine 60 mg/day and trazodone 200 mg/day. He continued in weekly cognitive–behavioral group therapy for a year and in a monthly relapse prevention group for a second year. The patient reported that with the combination of leuprolide acetate, fluoxetine, trazodone, and group therapy he had a suppression of all sexual fantasy and functioning, and, in particular, of all sadistic sexual interest and sexual and masturbatory fantasy involving boys. This suppression continued (1) after the leuprolide acetate was discontinued, at his request because of his dislike of the loss of sexual functioning, (2) after his fluoxetine and trazodone were stopped 3 months later, and (3) after the group therapy was discontinued a year later. On cessation of leuprolide acetate treatment, the patient required 4 months before restoration of sexual and ejaculatory functioning. On interviews annually thereafter over a 4-year period, the patient reported that his deviant sexual interests remained absent, although he had had a return to normal sexual functioning and consensual sexual relationships with adult males.

Table I. Depot-Leuprolide Acetate for the Treatment of the Paraphilias: A Report of 12 Cases

Patient	Age	Principal diagnoses	Duration (in months) of 7.5 mg of leuprolide	Outcome	Side effects noted
1	40	1. Pedophilia 2. Recurrent major depression 3. Alcohol, cocaine, opiate dependence 4. Borderline personality disorder	10	Markedly reduced deviant sexual arousal 4 years after leuprolide was discontinued	Loss of ability to ejaculate and have erections; 4 months until sexual function returned after depot-leuprolide was discontinued
2	31	1. Exhibitionism 2. Sexual disorder NOS 3. Recurrent major depression 4. Alcohol dependence 5. ADHD	10	Markedly reduced deviant sexual arousal 2 years after leuprolide was discontinued	Loss of ability to ejaculate and have erections
3	48	1. Exhibitionism 2. Voyeurism 3. Bipolar Type II 4. Alcohol dependence	6	Markedly reduced sexual arousal	Loss of ability to ejaculate and have erections, mild nausea, and vomiting
4	28	1. Pedophilia 2. Borderline intellectual functioning 3. Borderline Personality disorder	57	Markedly reduced sexual arousal	Loss of ability to ejaculate and have erections; mild to moderate demineralization
5	20	1. Pedophilia 2. XYY karyotype 3. Conduct disorder NOS	11	Markedly reduced sexual arousal and sadistic sexual fantasy	Loss of ability to ejaculate; ability to have erections maintained
6	42	1. Sexual masochistic disorder 2. Alcohol abuse 3. Recurrent major depression	11	Markedly reduced sexual arousal and interest	Mild gynecomastia; loss of ability to ejaculate and have erections; developed depression after leuprolide initiated
7	39	1. Sexual disorder NOS 2. Severe mental retardation 3. Psychotic disorder NOS	57	Cessation of aggressive sexual behavior	Mild gynecomastia; loss of ability to ejaculate and have erections; mild to moderate demineralization

8	36	1. Public masturbation 2. Exhibitionism 3. S/P closed head injury with left frontal lobectomy	9, 6, 4 at 7.5 mg/month; 9 with 3.75 mg/month	Reduced sexual arousal; cessation of exhibitionism and public masturbation	Decreased ability to ejaculate and have erections; however ability to have both was maintained
9	33	1. Exhibitionism 2. Pedophilia	9, 5 at 7.5 mg/month; 3 at 3.75 mg/month	Reduced sexual arousal, exhibitionism, and frotteurism	Loss of ability to ejaculate and have erections
10	47	1. Pedophilia 2. Alcohol dependence 3. Recurrent major depression	16 and 11	Reported loss of sexual arousal and interest	Loss of ability to ejaculate and have erections
11	37	1. Pedophilia 2. Voyeurism 3. S/P closed head trauma 4. Depressive disorder NOS	35	Patient and staff reported decreased sexual arousal and preoccupation	Loss of ability to ejaculate and have erections; statistically significant demineralization compared with baseline bone density evaluation
12	25	1. Exhibitionism 2. Frotteurism 3. Voyeurism	12	Patient and staff reported decreased sexual interest	Unilateral gynecomastia; loss of ability to ejaculate and have erections; 3 months until sex functioning returned

Patient #2 was a 31-year-old male diagnosed with exhibitionism, public masturbation, voyeurism, and compulsive use of prostitutes and peep shows. In addition, he had diagnoses of alcohol dependence and marijuana dependence, with abstinence and the use of 12-step programs for 7 years prior to his initial evaluation, and of recurrent major depression. Two years of weekly treatment with a cognitive–behavioral therapist had failed to control his deviant sexual impulses. He could not tolerate sertraline at a dose of 50 mg/day because of gastrointestinal side effects. He was started on oral medroxyprogesterone acetate tablets, preferring oral medication to intramuscular injections, 40 mg/day, while increased to 120 mg/day, with his wife observing his daily ingestion of medication; he remained on this medication for a 3-month period with his testosterone level going from a baseline of 233 ng/dl (normal being 194–833 ng/dl) to 178 ng/dl after 1 month of medroxyprogesterone acetate, 40 mg/day, and 148 ng/dl after 2 additional months of 120 mg/day. He was arrested for exhibitionism after 3 months of treatment with the medroxyprogesterone acetate and ultimately sentenced to 3 years of probation. After the 3 months of medroxyprogesterone acetate therapy and his arrest, he was started on depot-leuprolide acetate, 7.5 mg intramuscularly monthly, which he remained on for 10 months. His testosterone lowered to 27 ng/dl 2 months after the leuprolide acetate was started. During the course of these antiandrogen treatments he was involved in a weekly cognitive–behavioral group during which he learned techniques of masturbatory satiation and covert sensitization. After he discontinued the depot-leuprolide acetate, he reported having more control over all aspects of his deviant sexual behavior. He has continued for 2.5 years in a monthly relapse prevention group with markedly reduced deviant fantasies and reported deviant behavior and with otherwise normal heterosexual interest and functioning.

Patient #3 was a 48-year-old male with exhibitionism and voyeurism who also had a history of alcohol, marijuana, and cocaine dependence, and a bipolar type II disorder. He had been abstinent from all drugs and alcohol for 4 years at the time of evaluation. He had been maintained for several years on clomipramine 150 mg/day, valproic acid 1500 mg/day, paroxetine 60 mg/day, and naltrexone 50 mg/day. He had been previously treated with depot-medroxyprogesterone acetate, 200 mg intramuscularly weekly, for several years, which had been discontinued 3 years prior to the initial evaluation during a transition of psychiatrists. For 8 years prior to the initial evaluation he had also continued in a weekly supportive and cognitive–behavioral group for individuals with paraphilias. He began impulsively exposing himself after the medroxyprogesterone acetate was discontinued and was ultimately arrested. He was treated with depot-leuprolide acetate, 7.5 mg monthly, added to the regimen mentioned earlier, with a report of cessation of exhibitionistic impulses, which has continued for 6 months. His testosterone level dropped from a baseline of 950 ng/dl (normal being 260–1000 ng/dl) to 34 ng/dl. The patient said that his control of his exhibitionistic impulses on the leuprolide acetate was far

better than on the previous regimen, which relied on depo-medroxyprogesterone acetate instead of depot-leuprolide acetate, in addition to the other medications.

Patient #4 was a 28-year-old male who had been institutionalized in a state mental health system for 5 years at the time of initial evaluation. He had diagnoses of borderline personality disorder, cerebral palsy, and borderline intellectual functioning. He had had a history of pedophilia since his teens with numerous arrests and probation. He persisted with this deviant arousal despite masturbation satiation therapy, lithium, and sertraline. He initiated a lawsuit against the state government to permit him to have antiandrogen treatment and after assessment was started on depot-leuprolide acetate, 7.5 mg monthly. He reported the disappearance of all sexual functioning and fantasies, including those involving children. He remained on 7.5 mg of leuprolide acetate for 4.5 years, and was transitioned into a halfway house on the grounds of the state hospital where he was cared for. The patient was transferred back to a locked unit because of suicidal ideation, but he continued to report no sexual interest or arousal toward children and plans were continually being made to place him in a supervised community residence. The patient's baseline testosterone was 399 ng/dl (normal was 225–900 ng/dl); 3 weeks after his initial injection of leuprolide acetate his testosterone was 38 ng/dl; at 2 years his testosterone was 55 ng/dl; and at 3 years it was 27 ng/dl. The patient did not have a bone density evaluation until 4.5 years of therapy had elapsed; this showed mild to moderate osteopenia. The patient elected to continue with the depot-leuprolide treatment, calcium supplementation, and bone density evaluations every 6 months.

Patient #5 was a 20-year-old male with the XYY karyotype, conduct disorder not otherwise specified, and depressive disorder not otherwise specified and who had been a resident for several years in a residential treatment facility. He had a history, for many years, of recurrent sadistic pedophilic fantasies involving young males, without any overt behavior. His history of sadistic fantasy interfered with placement of the patient in a less-restrictive facility. A trial of sertraline up to 200 mg/day had no effect on this fantasy. A trial of depot-leuprolide acetate, 7.5 mg monthly, resulted in the suppression of such fantasy, and indeed, of all sexual fantasies, such that a transfer from the intensive residential treatment facility into a community program was effectuated. The patient was able to be involved in a sex-offender-specific outpatient program that previously would not accept him. After 11 months of depot-leuprolide acetate therapy, he retained an ability to have an erection, but not to ejaculate. The patient's testosterone dropped from a pretreatment baseline of 541 ng/dl (normal 241–827 ng/dl) to 53 ng/dl at 1 month and 18 ng/dl at 2 months postinception of the depot-leuprolide acetate.

Patient #6 was a 42-year-old male with a history of recurrent major depression, alcohol abuse, exhibitionism, public masturbation, sexual masochism, and recurrent visits to prostitutes. He was a married heterosexual male and his sexual masochism and other disorders had been severely interfering with his relationship

with his wife. He could not tolerate sertraline and requested for depot-leuprolide acetate that he was started on at a dose of 7.5 mg monthly, and which resulted in the cessation of all deviant sexual interest or activity. The patient's pretreatment testosterone was 525 ng/dl (normal being 194–833 ng/dl); and his testosterone 2 months after leuprolide acetate inception was <20 ng/dl. After 3 months of treatment with the leuprolide acetate he became depressed and this responded to treatment with fluoxetine 60 mg/day.

Patient #7 was a 39-year-old male with severe mental retardation and a psychotic disorder not otherwise specified, who had lived in a residential treatment facility for the developmentally disabled for many years. He had a history of repeatedly exposing himself while on trips away from the facility and of abruptly approaching women or female staff and grabbing their breasts or buttocks forcefully on at least 10 occasions. He was thought not to be a candidate for behavior therapy because of his severe mental retardation. He was started on depot-leuprolide acetate, 7.5 mg monthly, and maintained on this for 4.5 years, with a cessation of all episodes of sexual assault or exposure. His testosterone before leuprolide acetate treatment was 578 ng/dl (normal 194–833 ng/dl), which after 4 months of treatment dropped to 35 ng/dl; at 1 year of treatment his testosterone was 8 ng/dl. A bone-density evaluation after 4 years of treatment showed mild to moderate demineralization.

Patient #8 was a 36-year-old male, who had had a severe head injury 11 years prior to the evaluation, with a left frontal lobectomy and who had a history of hypersexuality, exhibitionism, and public masturbation. Following rehabilitation for 6 years at inpatient head injury facilities, he returned home to live with his family. He had been on carbamazepine for a seizure disorder. Attempts had been made to treat him at eight outpatient psychiatric or brain injury programs but his participation in each had to be terminated because the patient inappropriately engaged in sexual relations with women in these programs, or engaged in public exposure or masturbation in the proximity of the programs. He was started on 7.5 mg depot-leuprolide acetate, monthly, which was continued for 9 months, when it was stopped at his request because of his development of a sexual relationship with an adult female. He continued off leuprolide acetate for a year and then stopped the sexual relationship with his girlfriend and again became hypersexual. He was started again on leuprolide acetate, which was maintained for 6 months, with good control of his sexual behavior, until he developed another relationship with a female, when it was again discontinued. He continued in this relationship for a year when again he stopped the relationship and again began to expose himself. He was started on 7.5 mg of leuprolide acetate which was continued for 4 months, and then decreased to 3.75 mg/month. On all doses of the leuprolide acetate he reported that he was able to have erections and ejaculate once a day or every other day, compared with an average of two or three times per day prior to or off leuprolide acetate. Baseline testosterone was not obtained; a testosterone level

after 5 months of 7.5 mg/month intake of leuprolide acetate was 36 ng/dl (normal was 241–827 ng/dl).

Patient #9 was a 33-year-old male with a history of pedophilic fantasy and exhibitionism as well as bipolar disorder and adult onset diabetes mellitus. Intensive inpatient treatment in a cognitive–behavioral program for pedophilia for 2 months failed to eliminate these pedophilic fantasies or his exhibitionistic behavior. He was also treated with lithium carbonate 1200 mg daily and sertraline 150 mg/day along with weekly cognitive–behavioral group therapy, again without succeeding at control of his deviant sexual behavior. Depot-leuprolide acetate, 7.5 mg monthly, was administered with suppression of pedophilic fantasies and behavior and of exhibitionism for a 9-month period; he remained during this time in a weekly cognitive–behavioral group. Unhappy with the side effects of the depot-leuprolide acetate he discontinued treatment and reappeared 3.5 years later, with complaints of exposing himself and of pedophilic fantasy. Leuprolide acetate again resulted in a decrease in this fantasy, but he discontinued it after 4 months because of the effects of loss of sexual functioning. He continued with a 12-step program for "sexual addicts" and with monthly meetings with a psychiatrist, and reported good control off depot-leuprolide acetate.

Patient #10 was a 47-year-old male with a history of pedophilic fantasy and behavior toward boys since his early teens. He had twice been arrested and prosecuted for felonies involving child molestation. He reported no arousal toward adult males or females. He had also been admitted approximately 30 times to various psychiatric hospitals for complaints involving principally his pedophilic arousal. He was alcohol dependent but had been sober for 23 years at the time of initial evaluation. He retained deviant arousal to young males in spite of fluoxetine intake of up to 20 mg/day. He also had a history of dysthymia. He was treated with depot-leuprolide acetate, 7.5 mg monthly, for 16 months. He reported a loss of all sexual interests. At the patient's insistence and against medical advice, but with notification of the personnel who lived and worked with him to supervise him, he stopped receiving the depot-leuprolide acetate injections and promptly relapsed, despite continual participation in a weekly cognitive–behavioral group for sex offenders. He was restarted on leuprolide acetate, with a decrease in his deviant arousal, but received a substantial prison sentence as a result of his most recent relapse.

Patient #11 was a 37-year-old male with a history of pedophilia since adolescence with repeated episodes and convictions for child molestation of prepubertal males. He also had a history of a severe head injury with coma at the age of 6. In prison he was involved in repeated altercations. He also had a history of alcohol dependence, cocaine dependence, and polysubstance abuse. He was discharged from prison to a psychiatric hospital because of reported high sexual arousal toward young males. He was treated with thioridazine up to 200 mg/day which did not affect his sexual interest or arousal and caused retrograde ejaculation, and was discontinued. He was then treated with clomipramine, 250 mg/day, for depression

and to decrease his sexual interest. Although he was continued on this for 3 years, it only moderately affected his sexual interest and arousal in young males. He was also treated with valproic acid 1000 mg po bid for his episodic aggression with apparent success and was continued on this throughout his treatment. Depot-leuprolide acetate, 7.5 mg monthly, was added to the clomipramine and valproic acid, and this regimen was continued for almost 3 years. His testosterone levels before treatment were 214, 148, and 192 ng/dl (normal being 240–830 ng/dl); the patient was evaluated for a low testosterone level with no evident cause found. After 5 months of treatment on depot-leuprolide acetate, 7.5 mg/month, his testosterone level was 10 mg/dl; the patient reported a complete loss of sexual interest and preoccupation with boys and staff observed a decrease in his expressed sexual interest. The patient had a bone density examination of his lumbar spine and hip pretreatment and after 3 years of depot-leuprolide acetate therapy; he had developed a statistically significant decrease in the bone mineral density of his lumbar spine and hip.

Patient #12 was a 25-year-old male with a history of exhibitionism, frotteurism, voyeurism, public masturbation, psychotic disorder NOS, and multiple rapes of women, who had been found not-guilty by reason of insanity for the crime of sexual assault. After incarceration for 3 years pending trial, he was committed to a state mental health facility. He reported continual preoccupation and sexual fantasy of raping and exposing himself to women, which was not affected by fluoxetine intake of up to 80 mg/day. He was started on leuprolide acetate 7.5 mg intramuscularly and maintained on this for 12 months. He reported a loss of all sexual functioning and interest, and in particular of the deviant sexual fantasy and arousal. However, he developed unilateral gynecomastia and complained of the loss of sexual functioning and discontinued the depot-leuprolide acetate. His testosterone went from a pretreatment level of 525 ng/dl (normal being 286–1511 ng/dl) to a posttreatment of 41 ng/dl at 1 year of treatment. It took 3 months after discontinuation of the depot-leuprolide acetate before the patient's sexual functioning fully returned. His gynecomastia had not returned 5 months after discontinuation of leuprolide.

DISCUSSION

These case studies support the contention that depot-leuprolide acetate can reduce sexual interest and arousal in individuals with paraphilias. This is in accord with the observed effects of leuprolide acetate on the sexual activity of men who receive this medication for prostatic cancer (Rousseau *et al.*, 1988), as well as the other studies reported earlier. Comparisons of leuprolide acetate with medroxyprogesterone acetate or cyproterone acetate suggest that there are less side effects, including less risk of hepatitis, thrombophlebitis, and gynecomastia (Smith *et al.*,

1985) and this is supported by these case reports. Leuprolide acetate was generally well tolerated. However, the occurrence of demineralization and osteopenia in all patients on prolonged depot-leuprolide therapy, that is Patients #4, 7, and 11, is of concern and is consistent with reports of osteoporosis and decreased bone density in patients receiving androgen depletion therapy (Daniell *et al.*, 2000; Townsend *et al.*, 1997; Wei *et al.*, 1999). This has led us to establish a practice of baseline and then periodic (every 6 months or yearly) bone density evaluations for patients on active leuprolide treatment, along with consideration or use of more aggressive treatments to reduce demineralization (Diamond *et al.*, 1998; Hornstein *et al.*, 1998; Surrey *et al.*, 1999). It is also noteworthy that Patient #6, while having had a history of recurrent major depression, became depressed after treatment with leuprolide acetate and this is consistent with reports of mood disorders in women treated with leuprolide acetate for endometriosis (Rachman *et al.*, 1999; Warnock *et al.*, 1998).

Although long-term treatment with anti-androgens might be necessary to continue reduced sexual arousal (Thibaut *et al.*, 1996), the use of leuprolide acetate for a shorter duration of treatment with a focus of helping an individual obtain control of his sexual impulses and behavior and make use of other treatment modalities is illustrated by some of the cases discussed previously (Patients #1, 2, 5, 8, and 9).

It is also noteworthy that two individuals with previously unremitting continuous deviant sexual fantasies and behavior reported a cessation of such fantasy and a feeling of control over themselves not only with the active treatment with leuprolide acetate, but also subsequently off leuprolide acetate (Patients #1 & 2). It might be that the leuprolide acetate allowed these patients to use other modalities to control their sexual impulses or that the leuprolide acetate had some more long-lasting effect. It is also notable that some of the patients discussed earlier had failed to obtain control over their deviant sexual impulses despite behavioral or other psychopharmacological treatments, including the serotonin-reuptake inhibitor antidepressants or clomipramine (Patients #1, 2, 3, 5, 9, 10, 11, and 12 had trials of one or the other of these two classes of agents) and the leuprolide acetate was able to give them effective control. Depot-leuprolide acetate was more effective than oral medroxyprogesterone acetate for Patient #2 in reducing his serum testosterone level and in helping him develop control over his deviant sexual impulses.

Also noteworthy is the effect that depot-leuprolide acetate had on normal sexual functioning. All patients had reduced or markedly reduced deviant sexual behavior or arousal; reduced normative sexual interest and functioning was likewise reported or evident in all. However, one patient, #8, who had had a left frontal lobectomy and had a very high sexual drive, continued in a sexual relationship with full sexual functioning, although at a reduced frequency, while on the depot-leuprolide acetate; another, Patient #5, age 20, reported continuing normal sexual

interest. Patients #4, 10, and 11 all had had deeply fixated patterns of pedophilic interest and had reported this interest exclusively before the depot-leuprolide therapy and, consequently, the loss of this interest represented the loss of all sexual interest. It was our impression that individuals with a high level of sexual drive before treatment with depot-leuprolide were most likely to report some continued sexual interest while on medication. Likewise, the youngest patient treated, #5, age 20, reported continuing sexual interest while on the depot-leuprolide. These observations are in accord with those of Heim (1981) suggesting that castration has a greater effect on individuals who are older and that the frequency of sexual thoughts before castration was predictive of the frequency of sexual thoughts after castration.

This study had obvious limitations. It comprises 12 different case reports of treatment under very varied circumstances and with a heterogeneous population. Laboratory measurement was not possible in a uniform and regular way. Assessment of efficacy depended on patient self-report as well as the report of untrained staff who were observing these patients. Objective assessments of sexual functioning and sexual interest patterns, using penile plethysmography were not performed.

The high comorbidity of the patients presented is consistent with other studies of individuals who are sex offenders (Raymond *et al.*, 1999) or have multiple paraphilias or paraphilia-related disorders (Kafka and Prentky, 1998). The comorbidity and complexity of these patients with multiple diagnoses that could impact on sexual arousal or control of sexual impulses complicate the analysis of treatment effects of any one modality such as depot leuprolide. Likewise the concomitant administration of verbal and supportive therapies as well as other psychotropic therapies confounds the analysis.

Finally, the assessment of treatment of patients with paraphilias has ethical limitations. Many of the studies of antiandrogens have limitations of small numbers or a design that does not involve the standard double-blind placebo controlled design used in so many drug studies (Gijs and Gooren, 1996; Rosler and Witztum, 1998). Indeed, the use of crossover or placebo-controlled designs where outcome variables could involve the victimization of individuals is problematic. The fact that many individuals with paraphilias are mandated for treatment under court order also complicates the prescription of these medications and the administration of informed consent, one aspect of which requires that consent for treatment be given without coercion (Appelbaum and Gutheil, 1991).

However, the promising effects of these agents for the treatment of the paraphilic disorders, as is suggested by this study, with not only the possibility of maintaining patients on these agents indefinitely, but also with the possibility of using them to effectuate control by engaging individuals in other therapies and eventually discontinuing the leuprolide acetate, merit further study. The occurrence of demineralization and other side effects noted here, however, suggest caution and

careful evaluation of both the effects and side effects of this new antiandrogen therapy.

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